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Kerala Journal of Ophthalmology is celebrating its 40th year in 2014. It gives me immense pleasure to bring out my first edition of Kerala Journal of Ophthalmology after taking over as editor on this momentous occasion. The age of our journal is clearly reflected in the maturity and content of the articles contributed by our members and patrons.

Our journal has stood the test of time for four decades. Many of us will be curious to know how it has evolved over the years. Dr. N. Radhakrishnan, one of our seniormost members, takes us through this eventful journey in his Guest Editorial.

Dr. Lingam Vijaya, Dr. Ronnie George and their team in Sankara Nethralaya have contributed immensely to understanding the epidemiology of Glaucoma in South India through their landmark epidemiologic studies. The review article, "Epidemiology of Glaucoma in South India", is the result of their efforts.

Leptospirosis is no longer a rare disease. However, ocular manifestations of this disease are still poorly understood. Dr.Rathinam, Aravind Eye Hospital, Madurai, an authority in Ocular Leptospirosis shares her experiences about this enigmatic condition.

I was fortunate to have a number of brain storming sessions with many of our members and senior faculty on suggestions to further improve the reach and quality of our journal. One significant highlight in their feedback was that ophthalmology was getting too compartmentalized and specialty articles were increasingly becoming Greek and Latin to the comprehensive ophthalmologist. To this end, I have started a new column titled, "Practical tips for the Comprehensive Ophthalmologist", which will be useful to all.

All of us, in the course of surgical practice, develop many innovations and surgical techniques, which may often go unrecognized and unknown to others in the fraternity. "Surgical Techniques" provides the platform for our members to showcase their surgical innovations to the entire ophthalmic community.

"Photo essay", a picture based representation of a clinical condition, and "Diagnostic and Therapeutic Challenges", a specialty case discussion by national and international faculty, are other highlights.

Last but not the least it is your journal and it is your feedback, your criticism that is going to take the standard of KJO even higher. We have introduced "Letters to the Editor", where you can voice your comments about articles and provide suggestions for forthcoming issues.

Let us not forget that we are safely positioned high in the skies because we are resting on the shoulders of "*giants*" who have tread through more difficult paths to help us reach where we are today. We wholeheartedly acknowledge the contribution of all our Gurus of KSOS before us and beseech their continued mentoring and blessings.

"आ नो भद्राः क्रतवो यन्तु वश्वितः" Let noble thoughts come to us from all sides

- Rig Veda

Jai KSOS!
Dr Ashok Nataraj
Editor, KJO

Guest Editorial

History of Kerala Journal of Ophthalmology

The history of KJO started from the day KSOS (Kerala State Ophthalmological Society) was formally launched on 22nd December, 1974, at Kochi, under the leadership of Dr. C. E. Oommen, President and Dr. P. T. Chacko, Secretary. Dr. K. E. Eapen, Little Flower Hospital, Angamaly was elected as the "BULLETIN" Editor. Unfortunately he could not continue as he had to leave for higher training abroad and Dr. Narayanankutty was entrusted the job. He published the first official publication of the KSOS that year and could release three Bulletins the next year. Dr. T. P. Ittyerah and Dr. K. Mahadevan followed as Bulletin Editors. Compared to contemporary journals of today, these Bulletins of the initial years had few pages with very little scientific content.

Dr. T. P. Ittyerah, in his second stint as Editor, converted the Bulletin into quarterly journal format and rechristened it, "Journal of Kerala State Ophthalmological Society". He managed to release four issues a year but the going was tough due to lack of funds and genuine scientific material. Following this, Dr. N. S. D. Raju took over for the next four years. He tried to improve the contents as well as the appearance of the journal and included a "Secretary's Column".

Dr. K. Krishnankutty was the editor for two years (1988-1990). He radically transformed the journal in many ways. He changed it to a book form. In the first year, he published six issues and in the second year, twelve issues, which was quite spectacular by any standards. He included many articles on innovations and instrumentation. He also published five special issues on Glaucoma, Squint, Contact Lens, Headache and Uveitis. The journal became very popular among general ophthalmologists and postgraduates not only in Kerala but outside the state also. This not only improved the journal quality but also significantly increased the membership of KSOS as ophthalmologists were willing to become members just for the sake of getting the journal and special issues.

Dr. P. I. Mohan followed him as the editor for the next one year. He reverted back to the quarterly format and continued to maintain the high standards set by his predecessor. Dr. K. Mahadevan, who followed him, continued the good work but the "Secretary's Column" went missing. By now, Ophthalmology was advancing and Dr. A. Giridhar, who took over next, started many new sections in the journal, like journal reviews and case presentations despite practical constraints.

Dr. S. Sasikumar was the next editor from 1999 to 2001 and along with the then KSOS President, Dr. N. Radhakrishnan was instrumental in starting the "KSOS Newsletter " to discuss organizational matters in a quarterly format. For the first time a "Journal Fund" was approved which was a welcome relief for subsequent editors. Dr. S. J. Saikumar, Dr. Thomas Cherian, Dr Meena Chakrabarthy, Dr. G. Mahesh and Dr. Gopal S.Pillai, who followed as editors, were well appreciated during their tenures.

As you realize now, the scientific mouth piece of KSOS has evolved in a great way from the humble, lean "Bulletin" to "Journal of Kerala State Ophthalmological Society" to the current "Kerala Journal of Ophthalmology" over a period of forty years. All of us must acknowledge the pioneering efforts of our past Editors who despite all odds could make KJO comparable to any journal of international repute. Let us all salute them.

I am grateful to my young friend, Dr. Ashok Nataraj, for entrusting me with this job and I request all past editors to send in their experiences and add anything which I may have inadvertently missed. I pray that the sincere efforts of our stalwart Editors will never be in vain and KJO will gallop to greater glory in the future.

JAI KSOS! JAI HIND!

DR. N. Radhakrishnan DO
Past President KSOS(1999-2000)
Past Secretary KSOS(1987-1991)

Major Review

Epidemiology of Glaucoma In South India

Manish Panday MS, Ronnie George MS, Lingam Vijaya MS

Introduction

Glaucoma is the second leading cause of blindness in the world.[1] In chronic diseases such as glaucoma, it is important to estimate the disease burden in the population to plan treatment strategies. This is mainly done by population based prevalence studies that give us an idea of the proportion of people with disease. If they are re-examined a few years later this gives an estimate of the incidence of disease. Incidence studies give a more direct estimate of disease development and are more likely to provide risk factors for disease over time. However, it should be kept in mind that estimates may differ in different population groups or geographical regions and may also be affected by differing methodologies employed in studies. It is noteworthy that four major studies are from South India[2-11] and form the bulk of evidence for glaucoma in India. Recently published reports on glaucoma incidence and risk factors from India form an important source of evidence and more reports are likely to follow in near future to better understand the disease in our population.[12]

Diagnostic definition of glaucoma in population based studies

The major population based studies reported from south India are the Vellore Eye Study (VES),[2] Andhra Pradesh Eye Disease Study (APEDS),[3-6] Chennai Glaucoma Study (CGS),[7-10] Chennai Eye Diseases Incidence Study (CEDIS)[12] and the Aravind Comprehensive Eye Survey (ACES).[11] However, disease estimates differ among them as they employ differing methodologies for estimating glaucoma in the population.

Notably the CGS and CEDIS along with APEDS have used the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definitions for glaucoma.[13] These have standardized the classification for glaucoma in population based studies. Briefly, glaucoma is classified according to three levels of evidence in ISGEO. In category 1 level, both structural and functional evidence are necessary. This requires a cup-disc ratio (CDR) or CDR asymmetry $\geq$ 97.5th percentile for the normal population or neuroretinal rim width reduced to $\leq$ 0.1 CDR (between 11 to 1 o'clock or 5 to 7 o'clock) with definite visual field defect consistent with glaucoma. Category 2 needs advanced structural damage (CDR or CDR asymmetry $\geq$ 99.5th percentile for the normal population) when subject cannot satisfactorily complete visual field test. In Category 3, glaucoma is diagnosed based on IOP$\geq$99.5 percentile for the population in case media haze obscures visualization of optic disc. Being in the same geographical location, APEDS used the CGS normative data for diagnosing glaucoma. Thus while we need to keep in mind the methodology employed to understand study result implications, all studies have given a much needed information in our population.

Methodology of population based studies from south India

The Chennai Glaucoma Study[7-10] was a population based prevalence study in subjects 40 years and above and was conducted from 2001-2004. Subjects were enrolled from 5 randomly chosen divisions from Chennai city and 27 contiguous villages from Kancheepuram and Tiruvallur districts. The study used ISGEO criteria to classify subjects with glaucoma and enrolled 3850 subjects from rural and 3934 subjects from urban cohort who were examined at the base hospital. The Chennai Eye Diseases Incidence Study[12] was conducted from 2007 to 2010 and re-examined the surviving cohort of subjects after duration of 6 years. A total of 6022 subjects could be contacted/information was available, of whom 590 were not alive. Of the eligible 5432 subjects, 4421 (rural:urban 2510:1911) underwent a similar comprehensive eye examination at the base hospital giving a response rate of 81.3%.

The Vellore Eye Study,[2] conducted 140 km away from Chennai, enrolled urban subjects between 30-60 years and was conducted in 1994. A total of 972 subjects were enrolled. A diagnosis of glaucoma required raised IOP with/without typical glaucomatous disc changes and corresponding visual field changes. This was one of first study reports on

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glaucoma prevalence from India.

The Andhra Pradesh Eye Disease Study[3-6] was conducted from 1996-2000. Subjects were enrolled from urban city of Hyderabad and 3 rural districts (Godavari, Adilabad and Mahabubnagar). Subjects were aged above 40 years and prevalence data was republished for 934 urban and 2790 rural subjects using ISGEO criteria.

The Aravind Comprehensive Eye Survey[11] was conducted from 1995-1997 and enrolled subjects from 3 rural districts. For glaucoma prevalence, a subset of 5150 subjects aged 40 years and above was included. Primary Open Angle Glaucoma (POAG) was defined as optic disc changes (VCDR>0.8 or narrowest NRR<0.2 or asymmetry >0.2 between eyes) with visual field damage; in those without visual fields, glaucomatous disc damage was considered sufficient for diagnosis.[11]

Prevalence of Glaucoma and Ocular Hypertension

Primary Open Angle Glaucoma (POAG)

The VES was one of the first studies to report prevalence of POAG as 0.41% (95% CI: 0.01-0.81), although it used a different criterion for diagnosis as described.[2] Both the CGS and APEDS showed an increased prevalence in the urban residence as compared to rural one. The CGS had an urban prevalence of 3.51% (95% CI: 3.04-4.0) as compared to 4% (95% CI: 2.74-5.25) in APEDS.6.8 Similar rates for rural cohort were 1.62% (95% CI: 1.42-1.82) and 1.6% (95% CI: 1.13-2.06) respectively.[6,7] The prevalence rates were nearly double in urban cohort at CGS. There were more diabetics and hypertensives in the urban population of CGS,[8] however no association of these to POAG was noted. The reported prevalence in ACES was 1.7% (95% CI: 1.3-2.1).[11] The lower prevalence in VES may be inherent to the study sample as only 48.5% of eligible subjects underwent visual fields and the upper age limit of 60 years. Diagnosis of POAG was based on IOP criteria in VES, although glaucomatous visual field defect was mandatory for diagnosis of POAG. Most population based studies have highlighted the fact that a majority of patients with POAG have IOP ≤21 mm Hg. Forty five (52.3%) of 86 subjects with POAG in ACES had IOP < 21 mm Hg.[11] On similar lines, majority (67.19%) of patients in rural cohort of CGS had IOP ≤ 21 mm Hg, although increased prevalence of POAG was noted if IOP> 21 mm Hg.7 In APEDS 70.3% POAG patients had IOP < 22 mm Hg.6 The mean IOP in rural cohort of CGS was significantly greater in POAG (17.93± 5.35 mm Hg) as compared to normals (14.29± 3.32 mm Hg).[7,8]

There is a reported increase in prevalence with age across studies as shown in Table 1. The prevalence of POAG increased from 0.63% at 40-49 years to 3.25% to 70 years and above in rural and from 2.25% to 6.42% in urban cohort. The Odds for POAG increased exponentially with age and was maximum in over 70 years age group (Table 2).

No gender differences were noted at CGS.[7,8] ACES noted an increased association with male gender (Odds Ratio [OR] 2.2, 95% CI: 1.3-3.8), though no other prevalence study notes the same.[11] No association to gender and myopia were noted in both CGS and APEDS, although ACES reported a significant association with myopia (OR 1.9, 95% CI: 1.2- 3.9).[6-8,12] No association of POAG to hypertension or diabetes was noted at CGS and APEDS.[6-8] Lifestyle changes and/or higher rates of diabetes/hypertension and genetic causes could possibly account for rural urban differences.

Common to all studies was a lack of awareness of their own disease in the population. More than 90% subjects in most studies were unaware of their disease.[6-8,11] All except one subject in rural cohort (98.5%, n=63/64) and 94.1% subjects (n=127/135) in the urban cohort (n=127) of CGS were diagnosed to have glaucoma in the study.[7,8] In APEDS, 95.1% (n=78/82) of the combined cohorts were diagnosed to have POAG in the study.[6]

Primary Angle Closure Glaucoma (PACG)

Varied classification systems especially in angle closure disease have been used in most population based studies. Primary angle closure as defined by ISGEO[13] is classified as:(1) primary angle closure suspect (PACS): eye where >180 degree of posterior trabecular meshwork is not visible on gonioscopy; (2) primary angle closure (PAC): PACS with peripheral anterior synechiae (PAS); (3) primary angle closure glaucoma (PACG): PACS with glaucoma as defined above. VES defined PACG as acute or chronic.[2] The latter was appositional (with raised IOP) or synechial (with PAS). Glaucomatous disc or visual fields were not mandatory for diagnosis of angle closure glaucoma. The prevalence of PACG was 4.32% (95% CI: 3.01-5.61) in VES and all were of chronic form.2 This prevalence was several times that of POAG and highlighted the high rates of angle closure, though the rates will be different for the currently used ISGEO system.

The rural cohort in CGS had prevalence of 0.87% for PACG (95% CI: 0.58-1.16), 0.71% for PAC (95% CI: 0.45-0.98) and 6.27% for PACS (95% CI: 5.51-7.03).9 The urban cohort had 0.88% prevalence of PACG (95% CI: 0.60-1.16), 2.75% PAC (95% CI: 2.01-3.49) and 7.24% of PACS (95% CI: 6.58-

8.02).10 (Table 3-4)

The rural cohort in APEDS showed a prevalence of 0.7% for PACG (95% CI: 0.4-1.1), 0.2% for PAC (95% CI: 0.02-0.35) and 1.5% for PACS (95% CI: 1.1-2.0).6 The urban cohort had 1.8% prevalence of PACG (95% CI: 0.88-2.70), 0.8% PAC (95% CI: 0.2-1.4) and 3.5% for PACS (95% CI: 2.3-4.5).6 (Table 3,4)

ACES reported a low prevalence of angle closure glaucoma.[11] However, their definition of 'occludability' was not defined. There may be differences in gonioscopic interpretation by an optometrist and a trained ophthalmologist. This may partly account for the differences noted.

The rural cohort had a female preponderance (3 times) of PACG whereas no differences were noted in urban cohort of CGS. The authors note that though females have a higher risk of angle closure glaucoma, the observed difference in urban cohort may be due to a small sample size (n=34).[10] The higher rates for PAC in the urban cohort were attributed to the older age (54.8 vs. 53.8 years).[10] Thus the rural population were masked from the effects of PAC due to earlier age at cataract surgery. Diabetes as a risk factor was noted in the urban cohort only. No association to hypertension was noted in both cohorts.[9,10]

All patients in rural cohort of CGS (n=34) were unaware that they had glaucoma.[9] One (2.94%) was bilaterally blind, with none unilaterally blind. In the urban cohort, 14.7% (n=5) were previously diagnosed; of these 2 were diagnosed as POAG elsewhere.[10] Two (5.9%) were bilaterally and 3 (8.8%) were unilaterally blind due to PACG.10 Only 2 of the 6 PACG urban cohort patients in APEDS had undergone PI prior to their participation in the study, the others were managed as open angle glaucoma.[6] Nearly 82.8% subjects with PACG were newly diagnosed at the time of the study suggesting a silent course for angle closure disease.[6]

There were differences in prevalence rates for PACS and PAC in APEDS as compared to CGS. The differences may have resulted due to different gonioscopic lenses used and/or subjective interpretation of same or an actual difference (APEDS used NMR-K two-mirror lens, CGS used 4 mirror Sussmann lens. Difference in skill sets of examiners could account for this difference. Gonisocopy in the CGS was performed by trained glaucoma specialists and could explain the higher detection rates for angle closure disease. Of the 5 subjects previously diagnosed to have PACG in CGS, 2 were diagnosed as POAG elsewhere.10 Of the 34 subjects diagnosed to have PACG, one was bilaterally blind in rural and 2 subjects (5.9%) were bilaterally and 3 (8.8%) were unilaterally blind in urban cohort. All patients in rural cohort of CGS (n=34) were unaware that they had glaucoma.[9]

Only 2 of the 6 PACG urban cohort patients in APEDS had undergone PI prior to their participation in the study, the others were managed as open angle glaucoma.[6] Nearly 82.8% subjects with PACG were undetected at the time of the study.[6]

Ocular Hypertension (OHT)

Varied reported prevalence of OHT in the population occurs largely due to differing definitions for OHT. Prevalence in VES was 3.08 % (95% CI: 1.98-4.19%) which was defined as IOP>21 mm Hg with open angles and no evidence of glaucomatous optic neuropathy or visual field changes.2 Prevalence in APEDS was 0.42% (n=7, 95% CI: 0.11%–1.12%) where OHT was defined as IOP ≥ 22 mm Hg.6 ACES reported prevalence of 1.1% (n=57, 95% CI: 0.84-1.4%).[11]

Secondary and pseudoexfoliation glaucoma

In ACES the prevalence of secondary glaucoma was 0.3%.[11] The age- and gender-adjusted prevalence of secondary open-angle glaucoma in APEDS was 0.11% (95% CI:0.01–0.46) in participants ≥ 30 years age.[5] In rural cohort of CGS, the prevalence of glaucoma in aphakia/pseudophakia was 1.38% (37 aphakes, 17 pseudophakes).[14] Blindness (defined as best corrected visual acuity (BCVA) <2/40 and/or constriction of visual field to $<10^0$ from fixation) was seen in 22.2% subjects with glaucoma (constituting 2.49% of aphakic/pseudophakic subset). Aphakia and IOP were noted as risk factors for glaucoma in multivariate analysis. Aphakes had significantly higher IOP than pseudophakes and had more proportion of subjects with pseudoexfoliation, possibly reflecting a complicated cataract surgery. These rates, the authors concluded, required a need to concentrate on quality of surgery and follow up for patients undergoing cataract surgery.

Pseudoexfoliation (PXF) is a known risk factor for glaucoma and its reported prevalence from India is between 3-6%.[6,15-17] The mean age in PXF subjects was higher by a decade in CGS and ACES. Of the 108 (16.7%) subjects with PXF in CGS, 14 (13%) had glaucoma.[15] In APEDS, glaucoma was seen in 3.02% subjects with PXF and was predominant with outdoor activities.[16] Prevalence of PXF in ACES was 6% and glaucoma was seen in 7.5% of these subjects.[17]

Incidence of Glaucoma

Till recently, VES was the only study providing some

evidence on the incidence of glaucoma in India.[18-20] It gave some insight on the rates of conversion of PACS to PAC and PAC to PACG. At 5 years, 11 of the 50 subjects with PACS progressed to PAC (22%, 95% CI: 9.80-34.2).[18] Progression was noted in bilateral PACS. Of the original 37 PAC patients, 28 were re-examined. Eight of these (28.5%, 95% CI: 12-45%) progressed to PACG.[19] There was a greater risk of progression in bilateral PAC. Seven of the 14 bilateral and 1 out of 14 unilateral cases progressed to PACG. Progression was noted in 1 out of 9 (11.1%) who underwent peripheral iridotomy as compared to 7 out of 19 subjects (36.8%) who refused. No case of blindness due to glaucoma or acute angle closure were noted.[19]

Twenty one of 28 OHT were re-examined at 5 years in VES.[20] Among untreated OHT, 17.4% (95% CI: 1.95-32.75) progressed to POAG. One patient from normal cohort also progressed to POAG. Thus the relative risk (RR) of POAG in untreated OHT was noted as 19.1 (95% CI: 2.2-163.5).[20]

Recently, the results of six year incidence of primary angle closure disease in Chennai Eye Disease Incidence Study were published.[12] Subjects with angle closure disease at baseline and bilateral aphakia/pseudophakia were excluded. Incident angle closure disease was noted in 134 (4.0%, 95% C.I. 3.3-4.7) subjects of the eligible 3350 subjects. Of these 88 (2.6%) were PACS, 37 (1.1%) had PAC and 9 (0.3%) had PACG. Significant risk factors associated were a higher IOP, smaller axial length, shallow anterior chamber depth, increased lens thickness, anteriorly placed lens and hyperopia. Biometric parameters were associated with a higher risk of angle closure disease. A relative higher incidence of primary angle closure disease of 14.2% (95% C.I. 9.7-18.5) in subjects with anterior chamber depth less than 2.5mm and of 18.5% (95% C.I. 6.3-30.7) in axial length less than 21 mm was noted. In thicker lenses more than 5.5 mm, risk of primary angle closure disease was 10.1% (95% C.I. 6.0-14.3). An interesting observation was a decline in angle closure disease in subjects above 60 years in concurrence with higher rates of cataract surgery in this age group.[12]

Implications for the population

Quigley et al[1] estimated an overall worldwide prevalence of glaucoma to be 60.5 million in 2010 and increasing to 79.6 million by 2020. However, glaucoma affects Asians disproportionately to that in Western population with an increased propensity for angle closure disease as compared to Caucasians. It is estimated that 87% of angle closure throughout the world would be contributed by Asians.[1] An estimated 11.2 million people are affected with glaucoma in India.[21]

These facts are especially important for our population as the higher rates for angle closure glaucoma are also associated with a higher risk of blindness in India. Blindness was more due to angle closure (20% for both rural and urban) than for open angle glaucoma in APEDS (11.1% rural, 2.7% urban).[6] CGS also reported a higher blindness for angle closure glaucoma (5.9% vs 1.5%).[9,10] More than 90% subjects were unaware of their disease in CGS. This is even when we expect the urban population to have better access to medical care and a greater awareness on these disorders.

There are some fundamental questions which we need to answer with the available evidence. This is especially important of glaucoma being a blinding, asymptomatic disease and without a perfect way to screen for glaucoma in the population. Intraocular pressure in itself has a low sensitivity and specificity for diagnosis.[21] Besides, glaucoma remaining undiagnosed despite an ophthalmic consultation done in past or was misdiagnosed was apparent in these studies.

In essence, we need a stepwise approach to effectively diagnose and treat the enormous amount of undiagnosed glaucoma in the population. The focus could start from an effective case detection to pick at least high risk cases or those with moderate to advanced glaucoma and gradually shifting focus to early glaucomas and/or ocular hypertensives. The best way forward initially is to effectively look for glaucoma during planned cataract surgery and to provide reasonable and effective treatment for same. An eye examination during cataract surgery may be the first and probably the last interaction the rural population has with an ophthalmologist and the opportunity needs to be used to its maximum use. Blood relatives of glaucoma subjects should be counselled for a comprehensive eye examination and an increased awareness and knowledge of glaucoma to the population is necessary. The high rate of blindness in subjects with glaucoma clearly undermines the need for same. Nearly 20.9% (n=18) were blind in at least one eye, of these 6 had bilateral blindness in ACES.6 An overemphasis on using IOP as a diagnostic criterion for glaucoma should be discouraged. All facilities providing cataract surgeries should be encouraged to maintain hospital records for random scrutiny and data so that possible loopholes in system can be plugged.

We also need to have an effective training mechanism. This possibly needs to start at the basic training level for postgraduate courses. Any postgraduate degree in ophthalmology should ensure an individual has the capacity and skills for a comprehensive eye examination. These

can partly be addressed by Continuing Medical Education (CME) and skill transfers in places needing support for same. Fortunately the basic infrastructure required is less and requires a good tonometer (Goldmann's Applanation), gonioscope (preferably indentation) and stereoscopic disc examination by a 90D or 78D lens. In addition, basic visual field testing is preferable.

Training modules should focus on postgraduate colleges and ensure that the faculty has the necessary skills to impart students. Some amount of basic funding and equipment should be mandatory for all postgraduate colleges. However, it is not essential to have the armamentarium kept under lock and key for as and when use. Training optometrists and vision technicians for basic glaucoma diagnosis is mandatory. In future, technology is expected to play a larger role in medicine. Teleophthalmology and distance learning may help improve the lacunae and may reduce the borders to receiving good medical care at reach.

Conclusions

The burden of glaucoma is huge and undetected according to available evidence and is expected to rise further with the aging population. Training skills are essential to diagnose and treat glaucoma before visual morbidity sets in and a significant impact on quality of life occurs. Otherwise, millions will continue to suffer with this blinding disease.

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Major Review

Ocular Myasthenia

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Myasthenia gravis is a chronic neuromuscular disorder, characterized by weakness and fatiguability of voluntary muscles. It particularly affects muscles innervated by cranial nerves, due to impaired synaptic transmission across the neuromuscular junction. Patients may display weakness of extra ocular, bulbar, and / or limb muscles. Weakness is exacerbated by repetitive or sustained contraction and transiently improved by rest or anticholinesterase medications. Ocular Myasthenia (OM) is a localized form of myasthenia clinically involving only the extra ocular, levator palpebrae superioris, and/or orbicularis oculi muscles.

Historical Perspective

The first report of a myasthenic patient in the literature is credited to Thomas Willis in 1672, though the nomenclature "myasthenia gravis" was not applied until over 200 years later[10].In 1877, Wilks reported absence of brainstem disease on autopsy of a young woman with bulbar palsy (i.e., dysarthria, dysphagia), generalized weakness, strabismus, and respiratory paralysis, resulting in death. The post mortem examination was normal and the symptomatology was consistent with myasthenia. Jolly in 1895 introduced the term "myasthenia gravis pseudoparalytica"(from the Greek mys = muscle and "asthenia"= weakness, and Latin "gravis" = heavy or weighty). Jolly was the first to suggest physostigmine as possible treatment for this disease, as well as the first to demonstrate muscle fatigue following repeated faradic (electrical) stimulation (Jolly test). Mary Walker (1934) administered an injection of physostigmine, to a patient with generalized myasthenia and observed a marked improvement in muscle strength. In 1935, Viets and Schwab described the use of intramuscular neostigmine (Prostigmin) for diagnosis of myasthenia.

Natural history

Autoimmune myasthenia affects all races and ages, with an incidence of 4 to 5 per 100,000. Incidence is age and sex dependant, peaking in young women and older men[9]. Fifty to eighty percent of patients presenting initially, with purely ocular symptoms and signs subsequently develop clinical generalized disease typically within two years[1].

If myasthenia remains ocular for at least three years, then clinical generalized disease is unlikely to develop[11]. Ten to twenty percent of ocular myasthenics will spontaneously remit, either permanently or transiently, with relapse after one or more years. While corticosteroid treatment produces a higher incidence of remission and improvement, there is no evidence that anticholinesterase medications affect the ultimate course of disease. Age, sex, and pattern of onset are not helpful in predicting the eventual course of myasthenia[12].

Physiology of Neuromuscular Transmission

Neuromuscular transmission is initiated by an action potential depolarizing the terminal membrane of the motor nerve axon. It elicits an increase in calcium permeability and release of acetyl choline (ACh) from specialized sites on the nerve terminal into the synaptic cleft. ACh molecules diffuse across the synaptic space, bind to their receptors, and depolarize the postsynaptic membrane.

The postsynaptic membrane is a convoluted structure, with Ach receptors (AChRs) located on the crests of the folds (about 1500 receptor sites per square micrometer) and acetyl cholinesterase in the clefts. Released ACh is rapidly eliminated from the synaptic space by simple diffusion and hydrolysis by acetyl cholinesterase, with neuromuscular transmission completed within milliseconds.

Spontaneous release of small quantities of Ach from single vesicles into the synaptic cleft results in localized, low-amplitude depolarizations of the motor endplate, called miniature endplate potentials (MEPP). Release of a large quantity of ACh from multiple vesicles elicits a larger depolarization, referred to as an endplate potential (EPP),which is usually sufficient to initiate muscle contraction. The amplitude of the EPP is proportionate to the amount of ACh released.

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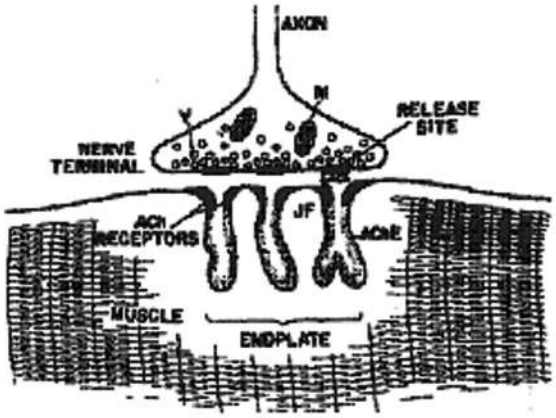


Diagram of the neuromuscular junction. Vesicles (V) release acetylcholine (ACh) at specialized release sites. After crossing the narrow synaptic space (arrow), ACh reaches the ACh receptors, which are most densely situated at the peaks of the junctional folds (JF). Acetylcholinesterase (ACh E) in the clefts rapidly hydrolyzes the ACh. M denotes mitochondria.

(Adapted from survey ophthalmology, vol 39 1994)

Normally there is a vast excess of both released Ach molecules and available postsynaptic AChRs in order to ensure optimal neuromuscular transmission. In addition, the amplitude of an EPP is four fold higher than that required to initiate muscle contraction. Thus, there is a safety factor, for neuromuscular transmission in normal EOM which prevents fatigue during repeated saccades. Any aberration that decreases the probability of interaction between ACh and its receptor, such as a reduction in the number of available AChRs in myasthenia reduces this "safety margin" and predisposes to failure of neuromuscular transmission, causing weakness and fatiguability.

Extraocular Muscle Physiology and Its Significance in Ocular Myasthenia

Extra ocular muscles (EOM) fibers have extremely rapid contraction kinetics and high firing frequencies of twitch when compared to other skeletal muscles[13]. The number of ACh receptors are less in EOM with lower quantities of ACh released[14]. These factors may increase EOM susceptibility to fatigue, particularly in myasthenia.

Multi terminal fibers of EOM (those that receive multiple synapses per fiber) may be more vulnerable to weakness and fatigue than single-terminal fibers which are found in most other muscles. Muscles with a predominantly tonic innervation, such as the levator muscle, tend to fatigue more easily during the day than the extraocular muscles. Other factor that makes EOM weakness particularly symptomatic, is that even slight fatigue of an EOM may misalign the visual axes and cause diplopia.

Pathophysiology

Circulating AChR Abs have been well-documented in numerous studies of patients with myasthenia, and these antibodies have been found in up to 87% of myasthenic patients tested. Antibodies to each of the subunits of the ACh receptor molecule have been found.

Major Antibody-Mediated Mechanism in the Pathophysiology of Myasthenia

1. Cross-linking and internalization of ACh receptors (accelerated degradation)
2. Damage to ACh receptors and postsynaptic membrane (probably complement-mediated)
3. ACh receptor blockade

Other auto antibodies:- Multiple auto antibodies other than AChR Abs have been identified in patients with myasthenia. Antibodies against skeletal muscle have been found in almost all myasthenic patients with thymoma and in about 30% of myasthenics without thymoma. Studies have reported thyroglobulin antibodies, antinuclear antibodies, antimuscle immunoglobulins, and rheumatoid factor in patients with myasthenia.

Cell mediated immunity:- Changes in populations of lymphocytes in the thymus of myasthenics, including a lower percentage of T cells and a higher percentage of B cells than normal and possible alterations in their antigenic properties, have been observed.

Histopathology:- Histopathologic studies in myasthenia have demonstrated postsynaptic changes in most or all patients, including a 70-89% decrease in the number of AChRs per neuromuscular junction in myasthenics compared with normal controls. Findings include sparse, shallow folds and marked simplification of the post-synaptic membrane, with widening of the synaptic clefts in many cases.

Associated thymic disorders:- Both thymic hyperplasia and thymoma have been associated with myasthenia. Thymic hyperplasia, characterized by infiltration of the thymus with lymphocytes and plasma cells and formation of lymph follicles (germinal centers), is found in as many as 65-70s of all myasthenics, particularly in younger patients.

Clinical characteristics

Ptosis and extraocular muscle palsies with fluctuating

diplopia are the hallmark of the disease. These signs are present sometime in the course of the disease in over 90% of patients with MG, whereas ptosis and diplopia constitute the presenting complaints in 70% of myasthenic patients[3]. If the weakness remains limited to extraocular muscles for 2 years, the chance of later dissemination is minimal[4].

Blepharoptosis is particularly suggestive of myasthenia if it is variable and worsens with fatigue or at the end of the day. Variability distinguishes this condition form others such as Horner's syndrome or third cranial nerve dysfunction. Ptosis may be unilateral or bilateral, though often asymmetrical. Ptosis may be elicited or worsened on prolonged upgaze, which is the basis for the lid fatigue test. Goerlick et al[6] made a useful observation on a method of enhancing myasthenic ptosis. First, the patient is instructed to maintain upgaze. As ptosis comes about, the examiner passively elevates the more ptotic upper lid, and over the next few seconds the other eyelid progressively falls, often to complete closure, sometimes with a few up and down oscillations. Cogan has labelled this phenomenon 'see saw ptosis'. In a myasthenic with bilateral ptosis, manual elevation of one eyelid reduces the effort required to raise that eyelid. Less effort is thus exerted by the contralateral levator muscle, and that eyelid becomes more ptotic, according to Hering's law.

Diplopia secondary to a paresis of the extraocular muscles is the second most frequent initial symptom. It usually, but not always, occurs with ptosis, and may mimic any disorder of eye movement, from paresis of an isolated eye muscle to a gaze palsy or complete external ophthalmoplegia. Muscles frequently involved are the medial rectus[5], inferior rectus and superior oblique, though any extraocular muscle may be affected. Paresis of upgaze is also common.

Special signs and symptoms in ocular myasthenia

Bells phenomenon:- Bells phenomenon of upward eye rotation on attempted eye closure may be absent in OM if the globe elevators are weak.

Cogan's lid twitch:- Cogan's lid twitch is a frequent finding in OM. If the eyes are rapidly returned to primary gaze from down gaze, the upper eyelid elevates excessively, i.e., a small overshoot occurs, and then either slowly becomes ptotic or twitches several times before returning to a fixed position. Cogan attributed this phenomenon to easy fatiguability and rapid recoverability of the myasthenic muscle.

Lid retraction:- In a patient with one eye myasthenic ptosis, the nervous system attempts to keep the eyes open by increasing the level of innervation to the ipsilateral and contralateral levator muscle (Herrings' law). Non ptotic eye also receives increased innervation and rises above the normal level since it is less involved by the myasthenic process. If the ptotic eye is covered, the retraction of the other eye ceases and the lids fall to the normal position. Because now the normal eye is determining the level of innervation to the two lids. As soon as the ptotic eye is uncovered, it will be observed to be much lower than it was, when that eye was determining the lid innervation. This test distinguishes this type of 'pseudo lid retraction' (due to ptosis of the fellow eye) from true neurogenic lid retraction. True neurogenic lid retraction occurs in upper mid brain or diencephalon lesions (Collier's sign). If the patient has true Collier's sign, the retracted lid will not fall when either eye is covered.

Nystagmus:- Although isolated nystagmus is uncommon, it may be seen unilaterally or bilaterally in myasthenics without an apparent ophthalmoparesis. The diagnosis of myasthenic nystagmus may be confirmed by resolution of the nystagmus following intravenous edrophonium injection[7].

Orbicularis oculi:- Weakness of the orbicularis oculi is often found in myasthenics and is evaluated by the examiner attempting to open the eyes against forced eyelid closure. The "peek sign" is due to orbicularis fatigue during gentle eyelid closure causing one or both eyes to gradually open spontaneously, and the patient appears to "peek" at the examiner. Despite orbicularis weakness, corneal exposure is rarely a problem. However, these patients may occasionally complain of tearing due to an inadequate blink. Orbicularis fatigue may also cause lower eyelid ectropion occasionally, seen typically during the latter part of the day.

Pseudo inter nuclear ophthalmoplegia:- Failure of the adducting eye beyond the midline and and dissociated nystagmus of the abducting eye on attempted horizontal conjugate gaze constitutes the syndrome of inter nuclear ophthalmoplegia. In some myasthenic patients this constellation of eye movements has been reported. It is important to distinguish myasthenia from a brain stem lesion. Intravenous tensilon resolves this condition in myasthenia but not in brain stem lesion. In myasthenia dissociated nystagmus builds gradually in amplitude, where as the nystagmus in true INO is present at its full amplitude at the onset and does not vary thereafter.

Pupil involvement:- Although some degree of pupillary dysfunction can occur in patients with myasthenia, in most patients this dysfunction is not clinically significant. In

patients with nonspecific ocular motility disturbances and clinically normal pupillary responses, myasthenia should be strongly considered in the differential diagnosis. Conversely, when oculomotor disturbances occur in the setting of a dilated, poorly reactive pupil, myasthenia should not be considered a likely cause[9].

Saccadic eye movements:- Eye movement recordings are useful in documenting the disorders of ocular motility. Four types of are found in myasthenic subjects: normometric, hypermetric, hypometric and glissade-like. Normometric, hypermetric and hypometric saccades had normal velocity for the actual size of eye movements. They differed in that normometric saccade reached the target, hypermetric ones overshot, and hypometric ones fell short. Glissade-like saccades had normal velocity at the beginning but decelerated toward the end of the movement.

Quiver (twitch like) eye movements are small amplitude saccades that are frequently hypermetric and have maximum velocities greater than normal due to a central compensatory adaptation that occurs in some myasthenics. It has been suggested that these quiver eye movements may be pathognomonic for myasthenia[8].

Factors Influencing the Manifestations of Myasthenia:- A wide variety of endogenous and exogenous factors may affect the signs and symptoms of myasthenia, often resulting in worsening or even onset of symptoms. These factors include temperature changes (worsening with heat, improvement with cold), fever, emotional stress, viral illness, surgery, menstruation, pregnancy, immunization, infection, thyroid dysfunction, and a variety of drugs.

Diagnosis

Ocular Myasthenia should be considered in any patient with ptosis and/or diplopia, particularly with variability and fatiguability of muscle function. Symptoms tend to be worse at the end of the day. Exacerbation of muscle weakness after repetitive or sustained effort and improvement following rest are important features of this disease, as well as absence of pain, sensory loss, clinical pupillary involvement, or decreased vision. Old photographs are very helpful in documenting duration of blepharoptosis.

Edrophonium and neostigmine tests

The edrophonium (Tensilon), test has remained a first-line test for diagnosis of myasthenia since its introduction by Osserman and Kaplan in 1952. Edrophonium inhibits the enzyme acetyl cholinesterase and results in an increase in available ACh for the limited receptor population in myasthenia. Onset of action begins 30-60 seconds after intravenous injection. Since it is quickly inactivated by hydrolysis, the effects usually resolve within five minutes. It is given intravenously with blood pressure monitoring, and electrocardiographic monitoring, on occasion, when indicated. The dose of edrophonium chloride is 0.15 mg/kg in children and usually up to 10 mg in adults. For adults, a l-2 mg test dose is injected intravenously to watch for a positive or idiosyncratic response. If eyelid function or ocular motility has not improved within one minute, then the remaining 8-9 mg of edrophonium is injected. If there is an improvement in muscle weakness, the test is recorded as positive and is concluded.

Neostigmine is a longer-duration anticholinesterase than edrophonium, permitting a lengthier evaluation of changes in ocular motility and eye alignment. Neostigmine is particularly useful in childen and patients with minimal ocular manifestations.



(Courtesy to Dr. Ani Sreedhar for clinical photographs)

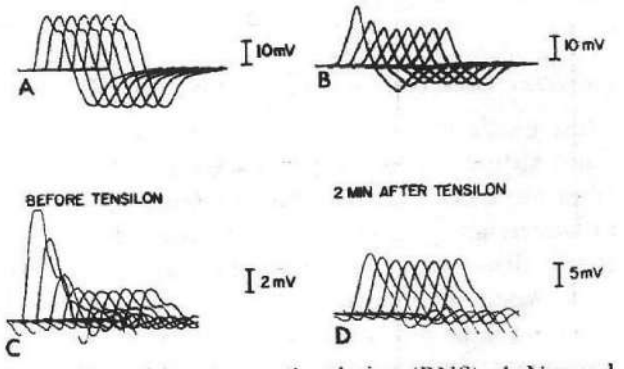
Before neostigmine After neostigmine

Sleep test:- The patient is kept in a quiet, darkened room and instructed to close his eyes and rest for 30 minutes. The patient is photographed and ocular motility measurements are obtained before and after the rest. The test is considered positive if there is improvement in the ptosis and/or ocular motility disturbance following the rest. This test is especially useful in cases where an edrophonium test is technically difficult, e.g., poor venous access or in children, or in patients with relative medical contraindications to anticholinesterases (e.g., bradycardia or cardiac dysrhythmia).

Ice pack test:- Local cooling to eliminate ptosis in patients with suspected myasthenia is a rapid and simple test. The size of palpebral fissure is measured, and a surgical glove containing crushed ice is applied to more ptotic eye lid for 2 minutes. After 2 minutes the glove is removed and the size of palpebral fissure is again measured. The test is considered positive if the size of the palpebral fissure improves.

Electrophysiological studies

Repetitive Supramaximal Motor Nerve:- In myasthenia, a characteristic decrement (usually greater than 10%) in muscle action potential amplitude with repetitive stimulation is typically seen. The decrement generally begins with the second and typically plateaus by the fourth or fifth response.



Repetitive nerve stimulation (RNS). *A:* Normal patient. No decremental response. *B:* 40% decrement in muscle action potential amplitude during RNS in a patient with myasthenia. *C* and *D:* RNS in a myasthenic patient before (C) and after (D) Tensilon injection. There is a decremental response before Tensilon (C), but *no* decrement (normal) following Tensilon (D). Note the change in amplitude scale between the two recordings.[1]

Single-fiber Electromyography (SFEMG):- This test evaluates neuromuscular transmission in individual motor endplates. A single fiber electrode is placed into a muscle in a position where action potentials from two adjacent muscle fibers can be measured. The time interval between the firing of any two muscle fibers from the same motor unit displays variability called 'jitter," which is minimal in normal patients. Defective neuromuscular transmission, as in myasthenia, causes increased temporal variability. SFEMG is more sensitive than RNS in the detection of myasthenia.

Anti acetylcholine receptor antibody assay

An elevated AChR Ab titer is diagnostic of myasthenia. With newer assays, AChR Abs have been demonstrated in up to 98-99% of patients with generalized myasthenia

Muscle biopsy

Muscle (motor point) biopsy, with quantitation of available AChRs by binding of radio labelled alpha-bungarotoxin, is considered highly sensitive and specific, though this test is technically difficult. Muscle biopsy may be extremely helpful in patients with borderline or absent AChR titers and equivocal electro diagnostic or pharmacologic test results. In addition to quantitation of AChRs, muscle biopsy provides opportunity for ultra structural analysis of the motor endplate.

If symptoms or signs are present that suggest a diagnosis other than myasthenia, MRI of the brain and orbits with contrast should be obtained.

Treatment

Treatment for myasthenia may be classified into two groups. The first group, symptom therapies, may reduce symptoms but do not alter the immunological process in myasthenia. Consequently they do not protect the patient from myasthenic crisis. The second group consists of immune therapies which may be used to alter the course of the autoimmune process and have the ability to prevent myasthenic crisis.

Symptom therapies

Acetylcholine Esterase Inhibitors

Inhibition of ACh esterase maximizes the availability of ACh to the remaining AChR molecules, contributing to successful postsynaptic membrane depolarization. However, continued immune attack on the neuromuscular junction eventually leads to sufficient loss of active AChR molecules resulting in an inadequate number of remaining AChR molecules to depolarize the postsynaptic membrane even when an excess of ACh is available. In these circumstances, inhibitors of ACh esterase will have little to no beneficial effect. Cholinesterase inhibitors should be used with caution in patients with bronchial asthma, cardiac dysrhythmia, pregnancy, lactation, and prostatic hypertrophy. Since

many patients with OM fail to note significant benefit from treatment with cholinesterase inhibitors alone, adjunctive immunotherapy is often necessary.

Side effects of cholinesterase inhibitors include abdominal pain and diarrhoea most commonly, due to cholinergic stimulation of the gastrointestinal tract which can be reduced by the use of oral atropine or belladonna containing compounds.

Pyridostigmine (Mestinon):- Pyridostigmine is the most commonly used cholinesterase inhibitor. The duration of action is approximately 4 hours. Pyridostigmine is available in a 60 mg tablet, a 180 mg sustained-release tablet, and a liquid suspension (60 mg/5cc). A parenteral form (5 mg pyridostigmine bromide/cc) can be used to supplement oral doses or as a replacement for oral therapy. Therapy can be initiated at 30 mg p.o. t.i.d. and then increased as needed

Neostigmine (Prostigmin):- Neostigmine is available as neostigmine bromide in 15 mg tablets for oral use and as neostigmine methylsulfate for parenteral use in multiple concentrations. The duration of action of neostigmine is approximately 2-2.5 hours

Ambenonium:- Least frequently used for myasthenia, but it is occasionally used in patients who are intolerant to pyridostigmine or neostigmine.

Immunotherapy

Immunotherapy should be considered in all patients with myasthenia whether or not serum AChR Abs are detectable.

1. Immunomodulators

a. Corticosteroids:-They inhibit the release of immune cytokines such as interleukin-1 and -2, tumor necrosis factor and interferon-gamma which result in immunosuppression. In addition, corticosteroids influence the cell-mediated and humoral-mediated limbs of the immune system. In OM, 60 mg of prednisone is initiated. Once benefit is achieved, prednisone dosage can be slowly tapered to 20-30 mg (or less) on alternate days. Acute exacerbation of the myasthenic weakness on initiation of higher doses of oral corticosteroids has been reported frequently. These patients should be hospitalized for close monitoring during initial therapy .This initial worsening is attributed in part to an increase in AChRAb titer, may be preventable by pre treatment with intravenous gamma globulin.

Prednisone may be replaced with long term therapies, such as azathioprine, in both generalized and ocular myasthenia.

b. Cyclosporin:- Cyclosporin inhibits the production of interleukin-2 and other immune cytokines, leading to moderate immune suppression. It is useful in patients who cannot tolerate prednisone. Cyclosporin is available as an oral solution (100 mg/ml), a soft gelatin capsule (25 mg or 100 mg), or an intravenous formulation. For a loading dose, l0-15 mg/kg may be used. 5-10 mg/kg/day is adequate to maintain serum levels between 100 and 500 ng/ml and achieve a good therapeutic response in myasthenia. Cyclosporin has a large number of adverse effects, generally the most problematic of which is its nephrotoxicity.

c. Tacrolimus (FK506) is a calcineurin inhibitor just as cyclosporine. The drug inhibits the proliferation of activated T lymphocytes, but also acts on ryanodine receptor-mediated calcium release from sarcoplasmic reticulum in muscle cells. The drug has shown a beneficial effect in MG, and it represents an alternative second-choice drug for moderate to severe MG.

2. Cytotoxic Therapy

Azathioprine, a purine analog interfere with purine metabolism, eventually inhibitis DNA and RNA synthesis. Azathioprine is available as a 50 mg tablet and in vials for intravenous use. Although the conventional dosage of azathioprine is 3-5 mg/kg. Complications of therapy are chemical hepatits,bone marrow depression, stomatitis, gastrointestinal disturbances etc.

Mycophenolate mofetil is regarded as an alternative drug for mild MG. The drug has few and mild side effects and is easy to use both for patients and doctors.

Methotrexate should be used only when first-choice immunosuppressive drugs do not have sufficient effect. Methotrexate has a good and proven effect for other autoimmune disorders. It can be tried in selected MG patients with a marked functional deficit, because it is usually well tolerated.

3. Humoral therapy

Plasmapharesis:- AChR Ab titers can be successfully decreased with plasmapheresis. Removal of one plasma volume (5% of the body weight ill kilograms; 1.5-3 liters per exchange) will reduce antibody titers by 30-75% in the serum. Therefore, repeated exchanges over a short period of time are required to reduce the total IgG and AChR Ab titers significantly. Improvement is usually apparent 24-72 hours after treatment but may not be maximal until l-2 weeks

after a series of plasmaphereses. Complications include transient hypotension, cardiac arrhythmias, and, rarely, infections at the site of intravenous access.

Intravenous Gamma Globulin:- Pooled human gamma globulin has been reported to be of transient benefit in myasthenia. Its mechanism of action is currently unknown. Most regimens involve administering intravenously 0.4 grams of pooled human gamma globulin per kilogram body weight followed by a repeat treatment daily for 3-5 days. These treatments may subsequently be followed by weekly or biweekly infusions to maintain effect.

Monoclonal antibodies: Rituximab is a chimaeric monoclonal antibody that targets B lymphocytes through its binding to the CD 20 molecule. MG is a prototype of an antibody-mediated autoimmune disease, and so rituximab and B-cell depletion are a very promising treatment alternative. Rituximab should be reserved for patients with severe MG, where treatment with prednisolone and at least two other standard immunosuppressive drugs has failed. For milder MG, the risk of progressive multifocal leucoencephalopathy and other potential long-term side effects probably outweigh its therapeutic potential.

Coordinated Use of Immunotherapies

Immunotherapy of myasthenia may be divided into an induction phase and a maintenance phase. In the induction phase, the immunotherapies used for major symptoms of myasthenia are those that have a rapid onset of effect, even though they may have significant toxicity with long term use. In maintenance therapy, the emphasis must be on therapies with acceptable long term toxicity.

Thymectomy

Although rarely used in ocular myasthenia, thymectomy is generally recommended for patients with generalized myasthenia. Multiple studies have shown an increased chance of remission for at least one to three years after thymectomy.

Surgical correction

In cases of burned out myasthenia, surgical correction of ptosis can be done after neurological evaluation. In some of our patients with bilateral severe ptosis we have done frontalis sling surgery.

Future

New and more selective immunoactive drugs are marketed worldwide. These drugs are established as first- or second-line treatment for an increasing number of autoimmune and inflammatory disorders, due to their proven superior clinical effect. As pathogenesis differs in MG subgroups, the immunoactive treatment needs to be individualised. Subgroups of MG will respond differently to various treatment alternatives. In the future, the detailed evaluation of each MG patient will hopefully have distinct therapeutic consequences, so that the treatment regime is tailored according to the specific autoimmune dysfunction.

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Before surgery After surgery

(Courtesy to Dr. Ani Sreedhar for clinical photographs)

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Major Review

Uveitis and Leptospirosis

S. R. Rathinam DO, DNB, PhD, Saurabh Agarwal MD

Introduction

Leptospirosis is a reemerging waterborne zoonotic disease that is common worldwide, especially in tropical countries with heavy rainfall. Adolf Weil described the disease as an acute process characterized by splenomegaly, jaundice and nephritis [1-4]. The name Weil's disease came to signify severe leptospirosis characterized by diverse clinical findings such as fever, jaundice, acute renal failure, refractory shock, and pulmonary hemorrhage. However milder form of leptospirosis or subclinical infection is more common than its severe Weil's disease. Suspicion of diagnosis becomes easy in the epidemic settings with a focused history, however it is difficult to diagnose leptospira disease in sporadic form[1-4]. Uveitis is an important ocular manifestation of leptospirosis in the latter immune phase of the disease[5]

Microbiology

Leptospires are highly motile, obligate aerobic spirochetes that share features of both Gram-positive and Gram-negative bacteria [1-4]. The organisms cannot be seen by direct light microscopy, Dark-field or phase-contrast microscopy of wet preparations is required for direct visualization of leptospires in cultures or clinical specimens. Silver impregnation method (Warthin-Starry staining), immunohistochemistry, or immunofluorescence microscopy can be used to visualize the organism in tissue. Ellinghausen-McCullough-Johnson-Harris medium (EMJH) is the standard medium for isolation of Leptospira from clinical specimen. Similar liquid or semisolid media include Korthof's, Fletcher's and Stuart's medium. Leptospires were originally divided into two groups, pathogenic leptospires grouped as "interrogans" complex and all other saprophytic strains were placed in the "biflexa" complex[1-4]. Based on molecular phylogenetic analysis, this genus includes twenty species, of which nine are classified as pathogenic, five as intermediately pathogenic, and six as nonpathogenic (saprophytic) The pathogenic and intermediate Leptospira species cause disease in humans and animals[4].

Epidemiology

Leptospirosis is a widely distributed zoonotic disease with incidence of human infection higher in the tropics than in temperate regions. The pattern of leptospirosis transmission can be epidemic, endemic or sporadic. Epidemic out breaks are common after rainfall or flooding. Endemic transmission occurs because of factors such as tropical humid environments and poor sanitation. Sporadic leptospirosis can occur among travelers, sewer workers, fish and poultry handlers, miners, butchers and tunnel digger. Human-to-human transmission does not occur but the most important sources of transmission to humans are rats, dogs, cattle, and pigs[1-4, 6].

Systemic leptospirosis

Leptospires can directly penetrate and infect humans through the conjunctival and possibly oral mucosa or through abraded skin. The organisms can escape innate immune defenses such as epithelial barriers, phagocytic cells, complements and enter into bloodstream or extracellularly within organs where they multiply. Then can spread hematogenously to all organs. Average incubation period is 5–14 days. Leptospires can be isolated from blood during the leptospiremic phase of 3–10 days [1,6].

Systemic Leptospirosis is a multi-system disease, the clinical picture depends on the organs involved. Anicteric systemic illness occurs in majority (85 to 90%) of the cases[7]. Pathognomonic ocular manifestations in the septicaemia phase include conjunctival chemosis and scleral icterus.8 Some develop icteric, septicemic leptospirosis or Weil's syndrome. The most notable feature of severe leptospirosis is the progressive impairment of hepatic and renal function. Renal failure is the most common cause of death. Common systemic clinical findings include any of the following.

- Abrupt onset of fever and rigor
- Intense headache, fatigue and prostration
- Muscle tenderness (calf and lumbar areas)
- Jaundice ,Conjunctival congestion without discharge
- Meningeal irritation, Delirium, psychosis
- Anuria or oliguria
- Multi organ hemorrhages and hypotension

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- Cardiac arrhythmia or failure, atrial fibrillation, flutter

The physicians easily miss the diagnosis, as symptoms are extremely variable, mimicking other infectious diseases. The differential diagnosis of systemic leptospirosis includes dengue fever, influenza, hanta virus infection, viral hepatitis, hemorrhagic yellow fever, malaria, typhoid, relapsing fever, meningitis, encephalitis and rickettsial disease [1-4] .

Leptospira completes its life cycle when it traverses the interstitial spaces of the kidney, the basement membrane of the proximal renal tubules, cross through proximal renal tubuloepithelial cells and become adherent to the proximal renal tubular brush border. After that, it is excreted in the urine. Chronic and persistent renal colonization can last for weeks or years. During immune phase, patient may develop uveitis, chronic aseptic meningitis, arthralgia, recurrent abortion or infertility. In second immune phase , appearance of antibody leptospires starts and only serology will be useful in this stage for the diagnosis[9].

Ocular Leptospirosis

Febrile illness usually lasts for about a week or two, Development of immunoglobulins in the plasma coincides with rapid immune clearance of the organisms. However, even after clearance from the blood, leptospires remain in immunologically privileged sites, including the renal tubules, brain, and anterior chamber of the eye, for weeks to months. Uveitis is an important late complication of leptospirosis. It may manifest after 2 days - 4 years of systemic infection, usually around six months. The onset and severity of leptospiral uveitis is variable, the severity does not correlate with the severity of systemic disease. It may occur as single or recurrent episodes. Leptospiral uveitis manifests as either anterior or diffuse uveitis. Anterior uveitis is usually insidious and mild in contrast to acute and relapsing pan uveal inflammation[5,9]. The spectrum of clinical manifestation of ocular leptospirosis includes,

- Interstitial keratitis
- Non granulomatous Iritis
- Hypopyon
- Cataract
- Vitreous cells
- Membranous vitreous opacities
- Papillitis
- Retinal vasculitis
- Cranial nerve palsies

Leptospiral uveitis is one of the common causes of hypopyon in leptospiral endemic areas. Although rare, pearly white, rapidly progressing cataract may be seen in leptospiral uveitis[10]. The posterior uveal involvement is more characteristic, vitreous reaction may be of grade one to four; vitreous exudates and veil like membranous vitreous opacities are the hallmark of the disease. They may persist for several months, even after the patient regains visual acuity of 6/6. Hyperemic disc and optic neuritis are more common than cranial nerve paresis, which involves third, fourth, sixth, and seventh cranial nerves. Retinal vasculitis with perivascular sheathing of the vein is commonly seen in leptospiral uveitis, however occlusion and neovascularisation are not common. Differential diagnosis of leptospiral uveitis include,

- Uveitis associated with ankylosing spondilitis
- Behcets syndrome
- Sarcoidosis
- Endogenous endophthalmitis
- Acute retinal necrosis

Patients presenting initially with unilateral uveitis with hypopyon and arthralgia can be misdiagnosed as HLA B27 associated uveitis and/or Behçet's disease. Severe vitreous reaction, vasculitis and hyperemic disc can differentiate leptospiral uveitis from HLA B 27 uveitis. Onset of Leptospiral uveitis is acute and of shorter duration, while Behcets uveitis is chronic, recurrent and insidious5. In addition, patchy perivasculitis is characteristic of leptospiral uveitis , in contrast to Behçet's vasculitis which is often occlusive. Although the fundus pictures of sarcoidosis very closely mimic leptospirosis, sarcoidosis is a chronic granulomatous uveitis with ocular features which can be differentiated from the acute non-granulomatous uveitis of leptospirosis. Syphilis, Lyme disease and leptospirosis are differentiated with the help of history of exposure to their respective risk factors and by specific serology. Rarely endogenous endophthalmitis can be mistaken for leptospiral uveitis and vice versa in tropical countries, specifically when the patient gives a history of systemic febrile illness prior to ocular disease[5,9].

Diagnosis

A high index of suspicion, exposure history and appropriate laboratory test are critical for confirmation of clinical diagnosis. Definitive diagnosis of systemic leptospirosis is possible only on isolation of the organism from the body fluids such as blood, urine or CSF. Isolation is possible during the early stage of illness, but successful only in 50% of cases [1- 4,11,12]. Antibodies are detectable after one or two weeks. The Micro Agglutination Test (MAT) is currently considered as the gold standard serological test where motile bacteria in liquid medium are treated with the titrated amounts of patients serum [1, 4] . When the serum contains

antibodies, agglutination occurs and can be seen under dark field microscopy. This test is highly specific even in endemic populations. However IgM-ELISA is commercially available and is less labour intensive than MAT. Diagnosis of systemic Leptospirosis is considered confirmed when there is a fourfold or greater increase in leptospira agglutination titer between acute and convalescent-phase serum specimens. The diagnosis is considered probable, if the clinical picture is compatible with leptospirosis and an agglutination titer is greater than or equal to 1: 200 dilution. Agglutination titer of greater than or equal to 1:100 dilution is considered significant in chronic cases as in leptospiral uveitis. Enzyme-linked immunosorbent assay, Indirect Hemagglutination, Dot-blot, and Lateral flow are other serologic tests on solid-phase assays, but has lower sensitivity compared to MAT.

Treatment

Early initiation of appropriate antimicrobial therapy in combination with supportive therapy reduces the mortality. Leptospires are sensitive to most antimicrobial agents including penicillin, amoxicillin, doxycycline and ceftriaxone. In practice, in severe systemic leptospirosis, intravenous penicillin G is administered at 1.5 million units every 6 hours for one week. Doxycycline may be given in doses of 100 mg twice daily for one week for mild to moderate cases 6. Steroids are the mainstay of treatment for leptospiral uveitis. The preferred mode of delivery depends upon the severity, laterality and anatomical location of inflammation[6,9].

Prognosis: The mild forms of systemic leptospirosis are much more common than the severe forms and most patients with the mild form tend to recover within 1-2 weeks. The mortality due to leptospirosis varies from less than 1% to more than 20%. Fatal outcome is mainly related to renal failure. Leptospiral uveitis carries very good prognosis.

Risk factors include:

- Occupational exposure - rice field workers, mining ranchers, abattoir workers, veterinarians, sewer workers, and military personnel
- Recreational activities - fresh water swimming, canoeing, kayaking, and trail biking in warm areas
- Household exposure -- Infestation by infected rodents and exposure to infected pet dogs, domesticated live stock1-4

Prevention

No vaccine is available for prevention of infection. Prophylactic antibiotic has a role depending upon the settings. It is beneficial for short termed, well defined exposures such as those involved in military training or recreational sports like swimming etc. Long term antibiotic therapy is not well established to work in high transmission endemic setting. General measures such as rodent and their infection control, self sanitation approach, avoidance of contaminated water reservoirs may be of use1-4. However long term and strict maintenance for such measure is difficult to practice in tropical countries.

Take Home Pearls

- Ocular signs are variable and mimic other uveitis entities, which makes the diagnosis difficult.
- Commonly presents as unilateral or bilateral acute, non-granulomatous pan uveitis
- Important clinical signs include hypopyon, optic disc edema, retinal vasculitis and membranous vitreous opacities.
- Although the systemic morbidity is high, leptospiral uveitis carries good prognosis.

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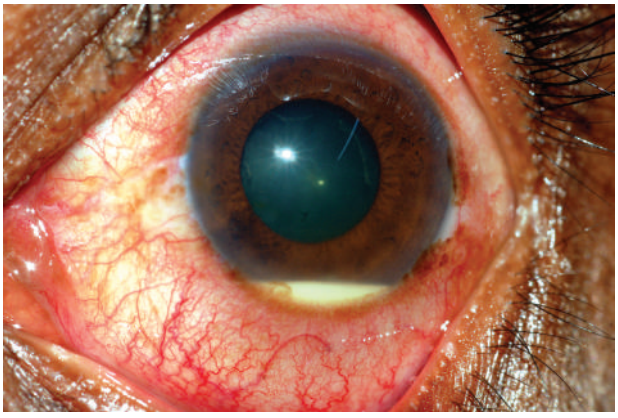


Fig 1: Hypopyon in leptospiral uveitis



Fig 2 : Rapidly maturing cataract with hypopyon in a young women with leptospiral uveitis

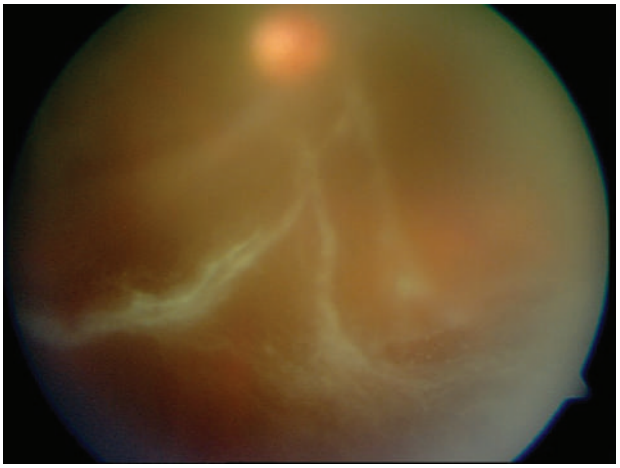


Fig 3 : Disc oedema with vitreous veil attached to the disc

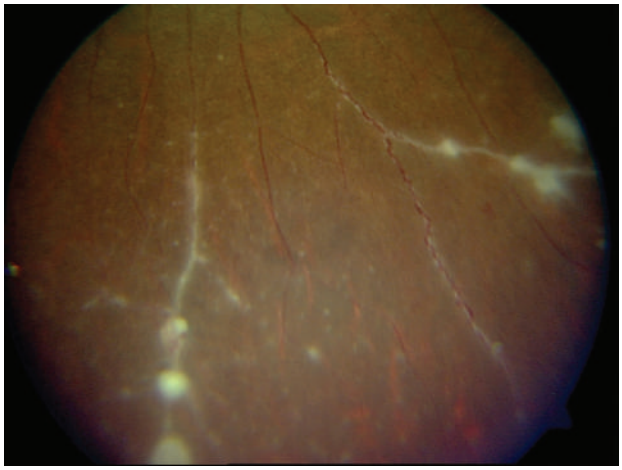
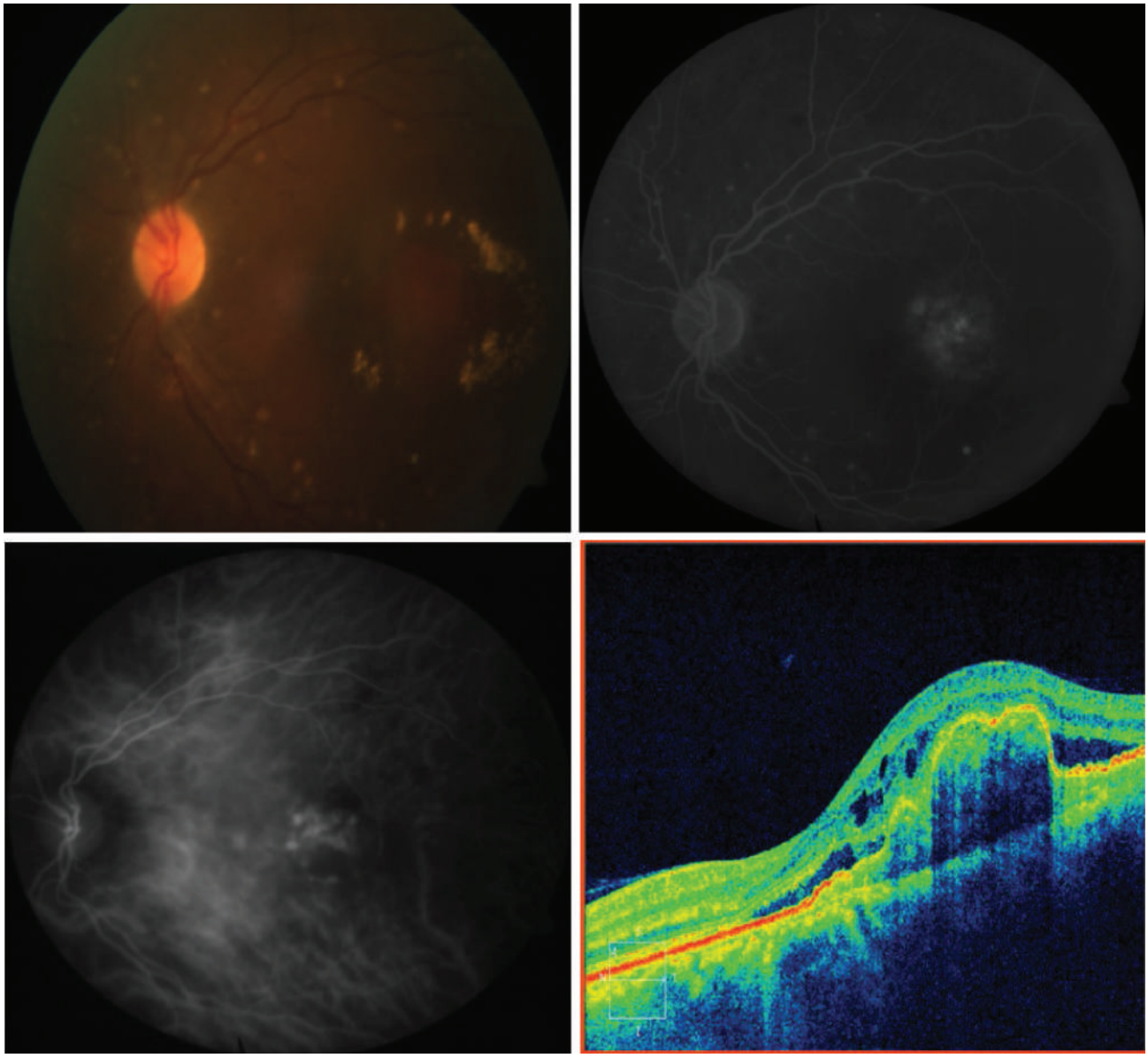


Fig 4 : Leptospiral retinal vasculitis

Identify the condition and what is the treatment?



Send your answers to: drashok.eye@gmail.com

The answer for the question in the last issue is
Lipemia retinalis and the enzyme deficient is lipoprotein lipase or Apo –CII deficiency
The winner was Dr. B. Jayaprasad, Amardeep Eye Hospital, Trivandrum

Original Article

Understanding Macular Telangiectasia

Unnikrishnan Nair R MS,FRCS, Manoj S DNB, FICO, FRCS, Sreelekha S MS, DNB, DO, FRCS Glasg, Rajna Rasheed MS, KGR Nair MS, FRCS

Abstract

Aim: To evaluate and assess the structural and morphometric changes that occurring in macular telangiectasia (MT) using Spectral Domain Optical Coherence Tomography (SD-OCT) and correlate these changes with visual acuity.

Methods: 250 eyes with clinically and angiographically confirmed Type 2 macular telangiectasia underwent imaging with Cirrus HD OCT. Various structural changes were noted including least foveal thickness, internal limiting membrane drape sign, hyper-reflective dots and plaques, inner and outer lamellar defects, signs of activity and vertical sliding down of retinal layers at areas of photoreceptor loss. These changes were correlated with the visual acuity. The independent sample Mann Whitney U test , the Chi-square test & Spearman's rho coefficient of correlation were used to evaluate the correlation between tomographic features and visual acuity.

Results: The least foveal thickness measured was 144.5 ± 43.4 μ(SD). This is statistically significantly less than normal foveal thickness measured on SD OCT as 227.64 ±11.74μ and the lab reference value of 247.89 μ. Other major features studied included inner lamellar defects (71 %), internal limiting membrane drape sign (37 %), central photoreceptor loss (94%), paracentral photoreceptor loss (87%), choroidal neovascular membrane (CNVM) (3.6%), vertical sliding of inner retinal layers (59.3%). There was a strong positive correlation (0.712) between decreasing temporal thickness and central foveal thickness.

Conclusion: Morphological and morphometric characteristics of the retinal layers as demonstrated by SD- OCT have a great bearing on visual prognosis and helps assess and understand the progression of macular telangiectasia.

AIM: To evaluate and assess the structural and morphometric changes that occurring in macular telangiectasia (MT) using Spectral Domain Optical Coherence Tomography (SD-OCT) and correlate these changes with visual acuity.

Introduction

Macular Telangiectasia (MT) or Idiopathic Juxtafoveal Telangiectasia (IJFT) is a macular disorder characterized by the development of juxtafoveal telangiectactic lesions leading to various structural changes in the retina which are mainly are of an atrophic nature but in the later phases may demonstrate exudative and neovascular phenomena. Pioneering work by Gass and Blodi[1] in 1993 led to a classification, that has stood the test of time, by subdividing IJFT into three distinct groups I, II, and III (also known as groups 1, 2, and 3), with two subgroups in each (A and B). This classification, based on clinical examination and angiographic findings, comprised additional staging of IJFT group II into five stages, the stages being 1. Loss of transparency or retinal whitening, 2. Macroscopically visible telangiectasia, 3. Presence of right angle vessels, 4. Pigment migration and 5. Sub-retinal neovascularisation (SRNV). These changes follow the logical temporal progression of the disease and even with the advent of newer multi modal imaging techniques these observations and pathogenetic mechanisms continue to be validated. Yannuzzi et al[2] proposed a simplified classification of IJFT, essentially a revision and simplification of the Gass–Blodi model. They proposed the term 'idiopathic macular telangiectasia' with two distinct types: Type 1 or 'aneurysmal telangiectasia' equivalent to IJFT group I (A and B combined), the second most common form of IJFT; and type 2 or 'perifoveal telangiectasia' equivalent to IJFT group IIA, the commonest type of IJFT. Foveal atrophy is the primary cause of the slow progressive visual loss occurring over years in these patients (to 20/200 or worse), distinguishable from the rapid and severe visual loss that may occur with the advent of SRNV and fibrosis. 1,2,5The five stages were simplified into two distinct stages that have clinical, prognostic, and therapeutic implications: nonproliferative stage (Stages 1–4), characterized by telangiectasis and foveal atrophy without SRNV, and proliferative stage (Stage 5 of Gass and Blodi) defined by the advent of SRNV and fibrosis.

OCT has provided great insight into the probable pathogenetic process involved in MT. Changes that have

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been evaluated in SD-OCT include decreased central foveal thickness, thinning and disruption of photoreceptor layer (PRL), presence of cystoids, lamellar defects, inner retinal reflective lesions, and intra-retinal and subretinal neovascularisation.

Materials and Methods:

250 eyes with clinically and angiographically confirmed MPT were included in the study. The study period was from March 2008 to December 2011. Institution review board and ethical committee approval of the study was obtained prior to commencement. SD-OCT (Carl Zeiss, Meditec, Inc., Dublin, CA) was done for each patient included in the study. Macular scanning was done using the 5 line high definition raster scan and the macular cube. Retinal co-morbidities like diabetic retinopathy, age related macular degeneration, etc., were all excluded from the study. Any eye where scanning was complicated by a hazy media was excluded from the study. No manual corrections were made. OCT images showing heavily distorted retinal architecture were excluded from further analysis, since no reliable results could be obtained.

Tomographic features studied included Least Foveal Thickness (LFT, measured manually), Central Foveal Thickness (CFT), Nasal and Temporal Perifoveal Thickness, Presence of internal limiting membrane (ILM) drape sign, change in reflectivity of retina/ disorganization of layers, Presence of hyper-reflective clumps or plaques, Central IS-OS loss (within 100 microns of centre of fovea), Para-central IS-OS loss (outside of 100 microns of centre of fovea), Collapse of retinal layers&Lamellar defects or cystoids. The patients were divided into two groups based on visual acuity .Group A where vision was better or equal to 6/12 and Group B where vision was worse than 6/12. Statistical analysis was done by SPSS version 16

Results:

The average age of the study population was 59.53 ±9.01 years. The average reported duration of the visual complaints was 19.87 months.

The mean log MAR visual acuity was 0.54951. For the purpose of statistical analysis, the eyes were divided into two visual acuity groups. Group A eyes had acuity better than or equal to 6/12 (< 0.301) while group B were eyes worse than 6/12 (>0.301). There were 135 eyes in Group A and 115 eyes in Group B.

Table 1 : Tomographic measurements (in microns)

Measurement	LFT	CFT	Temporal to fovea	Nasal to Fovea	Volume
Total Mean	144.52	187.99	260.28	275.06	9.294
Std Deviation	43.415	47.688	32.686	24.950	0.7029
Group A Mean	149.88	194.18	265.95	278.00	9.393
Group B Mean	131.35	183.20	255.89	272.79	9.217

Table 2 : Measurement of Horizontal and Vertical ISOS Loss(in microns)

	Horizontal ISOS loss	Vertical ISOS loss
Group A	1176.82	1113.52
Group B	1593.67	1570.76
Total	1430.56	1396.18
Std Deviation	923.588	1134.967

Table 3 : Grading of greatest linear measurement of ISOS Loss

(in microns)	< 500	500 - 1500	> 1500
Group A	20.0%	51.1%	28.9%
Group B	5.7%	25.7%	68.6%
Total	9.6%	34.6 %	55.8 %

Table 4 : Features and their frequencies

ILM Drape Sign	93	37 %	Vertical Sliding	148	59.3 %
Plaque Hyper Reflectivity	29	11.7 %	Change in reflectivity	183	73.3%
Dense intraretinal clumps	86	34.6 %	Inner Lamellar Loss	178	71%
Central ISOS Loss	235	94 %	Outer Lamellar Loss	110	43.8 %
Para-central ISOS Loss	218	87 %	Activity	9	3.6%

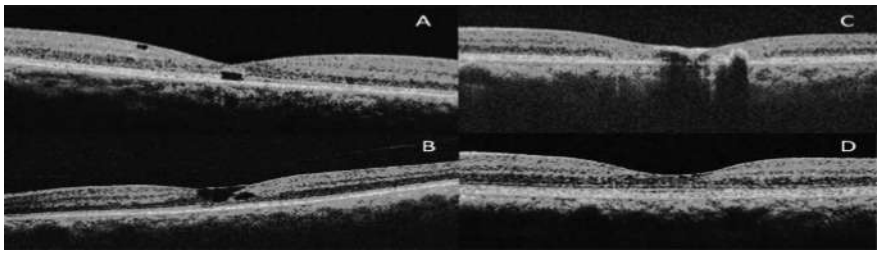


Figure 1: Tomographic Features in Macular Telangiectasia
A : Outer Lamellar Defects B: ILM Drape Sign C: Dense Pigment plaques causing Hyper-reflectivity D: Inner Lamellar Defects

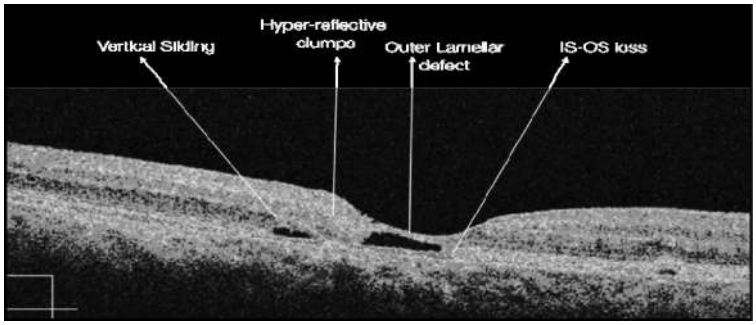


Figure 2 : Changes in the outer retinal layers in Macular Telangiectasia

Statistical analysis

The distribution of values of LFT and CFT was statistically different between the groups A an B according the independent sample Mann Whitney U test ($p = 0.014$& $p = 0.044$). The mean value of the LFT was statistically significantly different from the published normative data of foveal thickness value of 227.64μ and the lab reference value of 187.36 microns, according to Wilcoxon signed Rank test.The mean value of the CFT was statistically significantly different from the published normative data of foveal Thickness value of 227.64 microns and the lab reference value of 247.89 microns , according to Wilcoxon signed Rank test.The distribution of values of temporal thickness of retina temporal to fovea was statistically different between the groups A an B according the independent sample Mann Whitney U test ($p = 0.047$). However, there was no statistically significant difference between groups regarding volume and nasal retinal thickness. Spearman's Rho coefficient of correlation was used to evaluate the correlation between CFT, volume, nasal and temporal foveal thickness. It was found that there was a strong positive correlation between the change in temporal thickness and CFT (0.712).

The presence of following features was found to be statistically significant different in the two groups by Chi-square test.

1. Plaque like hyper reflectivity ($p = 0.012$)
2. Increasing amount of hyper reflectivity ($p = 0.046$)
3. Central ISOS loss ($p = 0.007$)
4. Para-central ISOS loss ($p = 0.001$)
5. Vertical Sliding of tissue ($p = 0.021$)
6. Change in reflectivity ($p = 0.015$)
7. Outer Lamellar defect ($p = 0.050$)

The greatest linear amount of IS-OS loss and the grading of IS-OS loss was found to be statistically significantly different in the two groups.

Discussion:

A study in 2005 by Paunescu et al[7]reiterated the following features with OCT- focal loss and disruption of the photoreceptor layer,cyst like structures in the foveola and within internal retinal layers such as the inner nuclear or ganglion cell layers, internal limiting membrane draping across the foveola related to an underlying loss of tissue, intra-retinal neovascularization near the fovea and central intra-retinal deposits and plaques.In 63% of cases, the presence of abnormal vessels and a discontinuity of the photoreceptor layer correlated with visual acuity. Studies,[8-15] including this one, have noted a lack of correlation between retinal thickening on OCT and leakage on fluorescein angiography. OCT characteristics correlate well with presumed histo-pathological processes in the disease. Retinal thinning, shortening of the photoreceptor outer segments and loss of reflectivity of the photoreceptor ellipsoid region were found in the central foveal region as well as the nasal and temporal perifoveal regions in eyes with MPT. This is presumed to be the cause for reduced vision. Cyst-like structures in the foveola and inner retinal layers are very common (50–100% of eyes with Stage 3 or

higher).[2,8,9,11,12,14-16] They are referred to as 'cystoids', have variable size, and are not seen clinically or on FA.[16] These may also be a sequel of progressive retinal tissue loss.[8,11,12] At the foveola, the inner lamellar cyst appears as a loss of tissue[2,9] with the ILM spanning across it and draping over it.9Intra-retinal neovascularization near the foveola, seen as highly reflective dots in the inner and outer nuclear layers16 is found in 21% of eyes.[9] Central intra-retinal hyper-reflective lesions that cause nonspecific posterior shadowing and correspond to hyper-pigmented RPE plaques are observed.[2,3]

All of the changes are consistent with the hypothesis of progressive retinal tissue loss, possibly due to Müller cells degeneration.[18,11] The latter could lead to alterations in the para-foveolar retinal capillaries, cause ILM separation, tissue loss, and cyst formation in the fovea.[3,8] Parallel to these changes, or later in the course of the disease, reduction of foveal thickness from resolution of foveal cyst or photoreceptor atrophy occurs.

In our study the eyes were divided into two visual acuity groups. Various parameters described by earlier studies were evaluated and noted and statistical analysis was done to find which features were more likely to bepresent in which group. The LFT and Central Sub-foveal thickness measurements were 144.53 $\pm$36.615μ and 187.99$\pm$41.68μ respectively. These values were found to be significantly different for the two groups. Also this value was compared to a normative data value of 227.64$\pm$11.74 μ obtained from a study by Carpineto et al.18and the lab reference value of 187.36 and 247.89 microns respectively .The values of the temporal subfield were also significantly different but there was no statistically significant difference between groups regarding volume and nasal retinal thickness. Correlation between the changes in foveal thickness and changes in nasal, temporal thickness and volume was computed. A significantly strong positive correlation was seen between the temporal and central thickness. This could be because the first pathological features of the disease are noted temporally even before central foveolar changes occur.

Visual loss is presumed to be due to the photoreceptor atrophy. The IS-OS loss was measured and graded. More significant and larger areas of IS-OS loss occurred in more visually advanced disease. In group A, a larger proportion of eyes (51.1%) had an IS-OS loss between 500-1000 μ, while in group B 68.6% of eyes had IS-OS loss of more than 1500 μ.

Of the tomographic features, the presence of the following features was noted to be different in the two groups i.e., presence of hyper-reflective plaques and increasing amount of hyper-reflectivity, central IS-OS loss & para-central IS-OS loss, collapse of retinal layers and change in reflectivity of outer retinal layers and presence of outer lamellar defects.

A few features are interesting to note:

1. The presence of outer lamellar defect was associated with poorer vision and not inner lamellar defects or the ILM drape sign.
2. Para-central IS-OS was more significantly associated with poor visual acuity than central IS-OS loss which was more common. This discriminant behavior may be the result of an increase in IS-OS loss with progression of the disease.
3. Collapse or sliding down of the retinal layers occur with increasing IS-OS loss and this may be indicative of a lack of vertical support to the inner retina when the photoreceptors atrophy.

Attempts at classifying the disease using OCT have been done extensively. Schutze et al19 divided eyes with MPT into three and Cohen11 et al proposed the a 5 stage classification for nonproliferative IJFT IIA , but these didn't correlate with visual acuity. Similar to observations by Charbel Issa,20 Wong noted that VA depended less on the presence of retinal atrophy, pigment migration or hypofluorescence signals per se, and more on their position relative to the foveal center. Central VA is decreased when these changes occur in the fovea, but may be preserved if they are limited to the parafovea.

Conclusion: Hence while proposing a classification, findings from our study namely the poor visual predictive indictors may be taken into consideration and a cluster or logistic regression model may be devised.

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Original Article

Clinical Outcome of Preoperative Intravitreal Bevacizumab Followed by Trabeculectomy with Mitomycin C for Treatment of Neovascular Glaucoma

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Abstract

Purpose: Trabeculectomy for Neovascular Glaucoma (NVG) is regarded as a challenging treatment with relatively poor success. Regression of anterior segment neovascularization preoperatively with intravitreal Bevacizumab (IVB) has lower likelihood of postoperative complications and failure of Trabeculectomy. We investigated the effectiveness of IVB on outcome of augmented Trabeculectomy in treatment of NVG.

Methods: 26 eyes of 24 subjects with refractory NVG were retrospectively analyzed. All patients had received IVB at least 1 week prior to augmented Trabeculectomy performed by a single surgeon. Average postoperative follow-up was 10 months. The main and secondary outcome measures were postoperative intraocular pressure (IOP) and visual acuity (VA) respectively. 'Complete' surgical success was defined as an IOP of </= 21 mmHg without medication while 'qualified' success was a similar IOP achieved with medication. Any subject having an IOP exceeding the defined success criteria was defined as 'failure'.

Results: Mean IOP reduction at 3 months postoperatively was 24.34mmHg ($p = 0.000$), with maintenance or improvement of vision by average of 0.41 log MAR units ($p = 0.017$). Using Kaplan- Meier survival analysis successful control of IOP was seen in 92.3%, 73.1% and 72.9% with or without medication, at 1 week, 1 month, and 3 months respectively. Postoperatively IOP lowering medications had to be continued in 65.4%. 27.1% failed to respond to treatment. Complications included Hyphema (66.7%), severe uveitis and Choroidal detachment (11.1% each).

Conclusion: Augmented Trabeculectomy with preoperative IVB in treatment of NVG gives good IOP control, providing a window period for evaluation and treatment of the predisposing posterior segment condition. Requirement of glaucoma drainage devices may be reduced. Maintenance of postoperative results may require multiple dosing of anti-VEGF and IOP lowering agents.

Aim of study: Trabeculectomy along with the use of adjunctives is regarded as the gold standard surgical therapy for most Glaucomas. However, in Neovascular Glaucoma (NVG) it is faced with relatively poorer outcomes due to aggressive neovascularisation and resultant bleb failure. Regression of anterior segment neovascularization preoperatively with intravitreal Bevacizumab (IVB) has a lower likelihood of postoperative complications and enhanced success of Trabeculectomy. This study was done to determine the effectiveness of IVB on the outcome of augmented Trabeculectomy in treatment of NVG.

Material and Methods

Subjects

This was a retrospective observational study of patients with refractory NVG who underwent IVB followed by trabeculectomy with Mitomycin C (MMC). The analysis included 26 eyes of 24 subjects. NVG in these patients was diagnosed by the presence of iris and/ or angle neovascularisation and an elevated intraocular pressure (IOP) of > 21mmHg. Informed consent was obtained from all patients after discussion about the potential benefits and risks of Bevacizumab and Trabeculectomy with MMC.

Patients with uncontrolled IOP on maximum tolerable medical therapy requiring filtering surgery and who underwent at least a single dose of preoperative IVB were included in the study. Those in whom IOP could not be recorded due to scarred corneas, or those who had undergone other IOP lowering procedures prior to Trabeculectomy, and those who were lost to follow-up were excluded from the study.

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Intervention

Preoperatively, the subjects underwent a comprehensive ophthalmic evaluation including visual acuity (VA), slitlamp biomicroscopy, IOP estimation by Goldmann applanation tonometry, Gonioscopy and dilated fundus examination. Those in whom media was clear enough for evaluation also underwent Fluorescein angiography to determine the extent of retinal ischemia and neovascularisation. The subjects were treated with atleast one dose of IVB at an average of 1 week prior to augmented trabeculectomy. Under local anaesthesia Bevacizumab (1.25mg/ 0.05ml; Avastin, Roche Pharmaceuticals, Basel, Switzerland) was injected intravitreally through the pars plana. After injection, anterior chamber paracentesis was performed as needed. Post injection, the patient was continued on IOP lowering agents. Regression of iris new vessels was looked for in all cases prior to surgery.

Subjects underwent Trabeculectomy with MMC application, performed by a single surgeon in all cases. A superior fornix based conjunctival flap was made. After fashioning a partial thickness triangular scleral flap, MMC soaked sponges with a dose of 0.4mg/ml of the drug was applied subconjunctivally and beneath the scleral flap for 3 minutes each, with care taken to avoid contact with the edges of the flap. The ostium was constructed using Kelly's Descemets Punch. No cautery was used to stop bleeding from the cut edges of the peripheral iris. The scleral flap and conjunctiva was sutured with 10-0 nylon which was removed at a subsequent visit.

Follow up

Patients were followed up on days 1, 7, 30 and 90 after surgery. The extent of rubeosis and functionality of the bleb were closely noted at each visit. The main and secondary outcome measures assessed were postoperative IOP and VA respectively. IOP was measured by applanation tonometry and VA using log MAR. Those in whom IOP continued to be above acceptable values were continued on topical IOP lowering medication. A 'complete' surgical success was defined as an IOP of </= 21 mmHg without medication while 'qualified' success was a similar IOP achieved with medication. Any subject having an IOP exceeding the defined success criteria was defined as 'failure'. The incidence and duration of postoperative complications (hyphema, vitreous haemorrhage, bleb leak, choroidal detachment, recurrence of neovascularisation, bleb infection/ endophthalmitis) was recorded.

Statistical Analysis

The rates of the outcome measures, viz. IOP and VA before and after surgery were compared using the Paired t test for continuous variables following normality assumptions and Wilkoxon Signed rank test for continuous variables not following normality assumptions. Success rates of IOP control were studied using Kaplan–Meier survival analysis. All analyses were performed using SPSS Version 16.0 for Windows. A p value <0.05 was considered to be statistically significant.

Results:

Twenty-six eyes of 24 subjects with NVG were retrospectively studied, with 2 patients having bilateral disease and both eyes being considered for analysis. The mean age of the patients was 61 years (range 36 -79 Years), among which 80.8% were males and 19.2% were females. The subject' demographic and basic clinical characteristics are summarized in Table 1. The mean preoperative VA was 1.71 log units (range ± 0.98) and IOP was 42.23 mmHg (range 26-68 mmHg). Evaluation of the anterior chamber angle revealed synechial closure in 42.3% eyes of which 23% had more than 2700 involvement. All patients required IOP lowering medications before surgery, with a mean of 3(range 1-5) medications.

Table 1: Baseline characteristics of study subjects

Characteristics	Mean /Frequency
Age	61 (36-79) years
Sex	
Male	21(80.8%)
Female	5(19.2%)
Number of affected eyes in patients	
Single eye	22(91.7%)
Both eyes	2 (8.3%)
Systematic Diseases	
Hypertension	9(34.6%)
Diabetes Mellitus	23(88.5%)
Ischemic heart disease	2(7.7%)
Associated Ocular disease	
PDR	20(76.8%)
BRVO with Proliferative retinopathy	1(3.8%)
Ocular Ischemic syndrome	2(7.7%)
CRVO	2(7.7%)
C/C post operative uveitis	1(3.8%)

Majority of the subjects had neovascularisation secondary to proliferative diabetic retinopathy (PDR) (76.8%), followed by vascular occlusions (19.2%). Regression of iris new vessels was noted in all cases prior to surgery. All patients underwent similar procedures. The average follow-up period was 10

months (range 1- 28 months). Using Kaplan- Meier survival analysis successful control of IOP was seen in 92.3%, 73.1% and 72.9% with or without medication postoperatively, at 1 week, 1 month, and 3 months respectively (Figure 1).

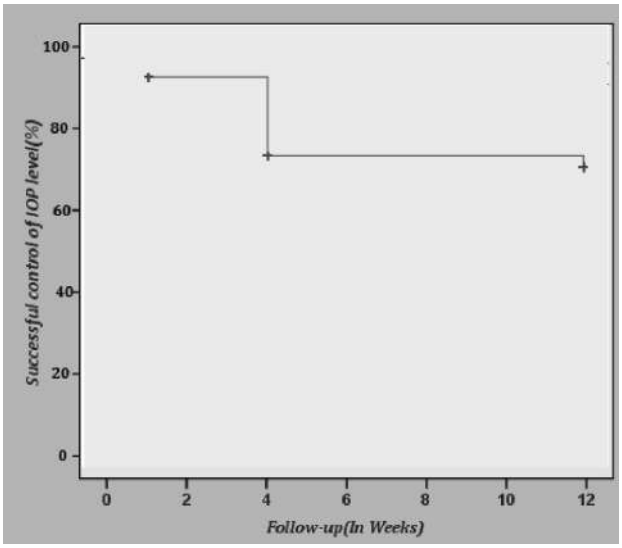


Figure 1: showing Kaplan–Meier survival curves of IOP success at each follow-up (1week, 1month and 3months).

Table 2: Pre- and Post- Operative Main Outcome Measures:

Characteristics	Mean	Mean Difference from Post operative Measurements	p value
IOP level(mm/mg)			
After 1 Week	12.85(6-26)	29.39	0.000*
After 1 month	18.96(10-54)	23.67	0.000*
After 3 Month	17.89(10-46)	24.34	0.000**
Last Follow Up	16.25(10-28)	28.94	0.000*
Visual Acuity (log MAR)			
After 1 Week	1.44±0.93	0.27	0.037*
After 1 month	1.42±0.98	0.22	0.035*
After 3 Month	1.3±0.96	0.41	0.017**
Last Follow Up	1.52±1.14	0.09	0.75**

* p value based on Paired t test
** p value based on Wilkoxon Signed rank test

The mean IOP reduction at 3 months postoperatively was 24.34 mmHg (p =0.000), with maintenance or improvement of vision by an average of 0.41 log MAR units (p =0.017) (Table 2). Postoperatively, 65.4% of patients required antiglaucoma medication by the 3rd month with a mean number of 2(range 1-3) medications. 27.1% of the subjects eventually failed to respond to treatment and required additional procedures. Intra- and postoperative complications included mild to moderate Hyphema (66.7%), severe uveitis and Choroidal detachment (11.1% each).

Table 3: Rates of success based on Post operative IOP:

	Follow-Up (Percentage)		
	1 week	1 month	3 month
Complete success rate (<21mmHg without medication)	76.9	52.3	34.6
Qualified success rate (<21mmHg with medication)	15.4	20.8	38.3
Failure rate (>21mmHg with/without medication)	7.7	26.9	27.1

Table 4: Complications intra- and post-operatively:

Complication	Number of Eyes
Hyphema	17
Severe Uveitis	3
Choroidal Detachment	3
Recurrence of Neovascularization	2

Discussion:

Glaucoma secondary to neovascularisation of the angle (NVA) continues to be a refractory disease with poor clinical and treatment outcomes. Ischemic conditions of the retina, such as diabetic retinopathy and vascular occlusions induce production of vasoproliferative agents leading to neovascularisation of the iris (NVI) and NVA with eventual intractable elevation of IOP.

In the present study, the incidence of the disease was seen to be much higher in males, with the commonest predisposing event being diabetic retinopathy, [1] thus stressing the importance of periodic dilated fundus examinations in suspicious cases and the assessment of retinal perfusion

with angiography. NVG following ischemic vascular occlusion have been found to be more severe compared to those following PDR. [1] Our study shows a relatively better postoperative outcome, probably because the number of subjects with PDR was much more, compared to ischemic vascular occlusion.

Tackling retinal angiogenesis in NVG with panretinal photocoagulation (PRP) to reduce the impetus for neovascularisation prior to filtering surgery had been the norm in the last decade. Using standard filtration techniques with preoperative PRP alone was found to have moderate immediate postoperative success in NVG. The success was limited by the significant inflammation and incomplete regression seen in these eyes postoperatively.[2, 3] Trabeculectomy with adjuncts like 5-FU and MMC in NVG showed better although unpredictable success rates initially which decreased long term with persistent neovascularisation, frequent recurrences and post op complications. [4, 5] Glaucoma drainage devices (GDD) have gained popularity in the surgical treatment of NVG, as their success is less dependent on control of intraocular inflammation and the failure of the bleb. Shen et al found similar postoperative outcomes with augmented Trabeculectomy and Ahmed Glaucoma valve in NVG eyes.[6]

Recent literature describes off-label use of Bevacizumab in the form of intracameral 7 or intravitreal injections to be effective in causing regression of ocular neovascularisation. [8] This is increasingly being followed as the treatment practice for rapid regression of anterior and posterior segment neovascularisation and of intractable macular edema, although the effects seem to be temporary. In NVG, this consequently has a beneficial effect on reduction of IOP in the presence of an open anterior chamber angle.[9, 10, 11] With extensive synechial closure of the angle, it is unlikely that antiglaucoma medications alone would control IOP after Bevacizumab injections, although Yazdani et al reported two cases of NVG with complete synechial closure to have a stable IOP after 6 months of repeated administration of IVB injections.[12]

Using Bevacizumab as an adjunct with trabeculectomy in NVG eyes seems to improve the relatively poorer surgical outcome as against when the latter is performed alone. The study by Saito et al on 50 NVG eyes suggested that preoperative IVB suppresses postoperative hyphaema and is effective in improving short-term postoperative IOP control following Trabeculectomy.[13, 14, 15] Analysis of subjects in the present study showed a successful control of IOP of 92.3% immediate post op which gradually declined by the 3rd month to 72.9% with or without medication probably due to the waning effect of Bevacizumab. The primary outcome measure of this study of reduction in IOP by an average of 24.34mmHg reaffirms that preoperative IVB is indeed a useful tool. The beneficial effect of the procedure was also evident in our second outcome measure of maintenance or improvement in VA by an average of 0.41 log MAR units.

The most common complication faced intraoperatively and in the post op period was mild to moderate hyphema (66.6%), described similarly by other authors.[15] A large number of patients (65.4%) continued to require antiglaucoma medications progressively, therefore we infer that repeated injections of IVB are required for sustained effect. The major cause of failure seen in 27.1% was recurrence of new vessels.

The inherent limitation of the study may be its retrospective nature and possibly the relatively small number of cases. Since anti VEGF agents have already been proven in its efficacy to reduce NVI, we used them in all our cases. Hence we do not have a comparative group of patients who did not receive IVB.

Conclusion:

Augmented Trabeculectomy with preoperative IVB in treatment of NVG gives good IOP control, providing a window period for evaluation and treatment of the predisposing posterior segment condition. Requirement of glaucoma drainage devices may be reduced. Maintenance of postoperative results may require multiple dosing of anti-VEGF and IOP lowering agents.

Although repeated injections are required to prevent recurrences, use of these in combination with other modes of therapy like retinal laser photocoagulation show promise in long term control of the disease.

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Original Article

Quantification of Energy Distribution During Torsional Phacoemulsification Using Videography

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ABSTRACT:

Purpose: To assess the steps involving generation of maximum energy during torsional phacoemulsification

Methods: 50 patients were randomized into four groups depending on their grade of nuclear sclerosis and subject to torsional phacoemulsification.The surgical procedures were recorded and the videos were analysed in segments depending on the steps of the phaco procedure. The energy expended during the steps were tabulated.

Results: The cumulative dissipated energy with a high correlation to the grade of cataract had maximum rise during the initial procedure of burrowing and segmentation of the nucleus.The energy expended during emulsification of the segments was comparable in all grades.

Conclusions: The energy expended in the system is most during dissembly of the nucleus. Efficient dissembly can thus lead to less energy generation.

INTRODUCTION

The energy produced in a closed system has the potential to produce undesirable effects which translate to damage to corneal endothelial cells, angle structures , iris and posterior capsule inside the eye. Though with the advent of non longitudinal modes of phacoemulsification like ozil and ellips, the efficacy of phaco has increased, the parameters on which the dissipated energy depends needs to be studied so that factors under the surgeons control can be better understood and therefore modified to produce optimum results.

AIM OF STUDY

Besides the grade of cataract, the technique of dealing with the nucleus of the cataract is likely to have a bearing on the amount of energy used in the system. We decided to study how these factors influence the energy output and how significant that influence is. We also wanted to know the energy expended for each nuclear density and phase of nucleus management in our hands.

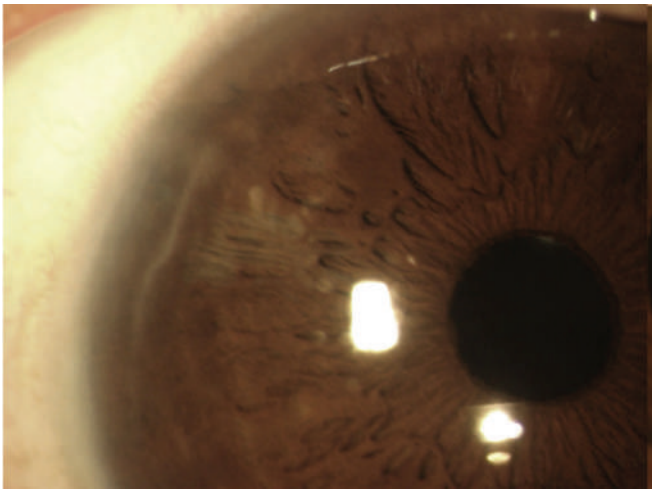


Fig.1 Iris chaffing

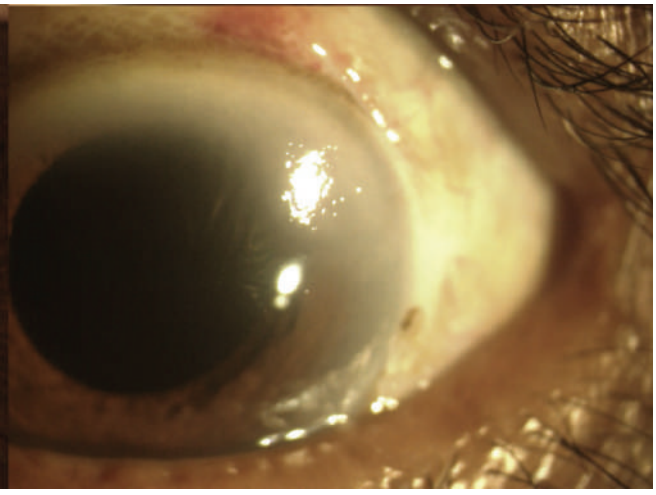


Fig. 2. Sectional corneal edema

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MATERIALS AND METHODS

This was a prospective randomized trial conducted on 50 patients who had cataract and underwent surgery with the Alcon Infiniti Vision System using Ozil technology.The patients signed an informed consent. The patients were subject to uniform preoperative medications, namely topical antibiotics, NSAIDs and mydriatics. All surgeries were performed by the same surgeon (SN).The incision was a 2.2 mm clear corneal superotemporal one, the position being the surgeon's preference. Depending on the grade of cataract on a scale of 1 -4, the machine parameters were adjusted. The initial ozil amplitude varied from 0 with a maximum of 100% in complete footpedal 3 down position. The vacuum was either panel or linear of upto 350 mmHg with a dynamic rise of 2. The aspiration flow rate varied from 30 – 40. A 0.9 miniflared 45 degree Kelman tip with Ultrasleeve(Alcon Lab Inc) was used. The technique of direct chop was used in all patients. The video recording of each case was

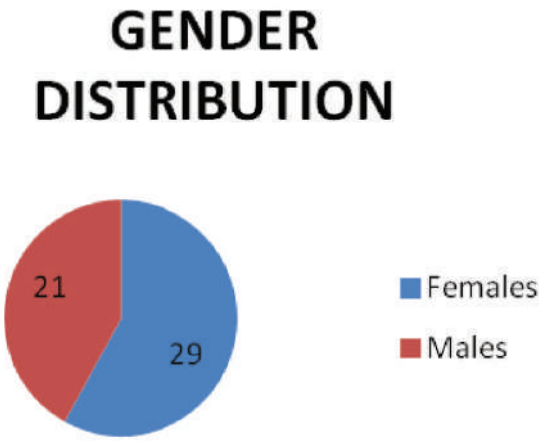


Fig 3. Gender distribution of patients

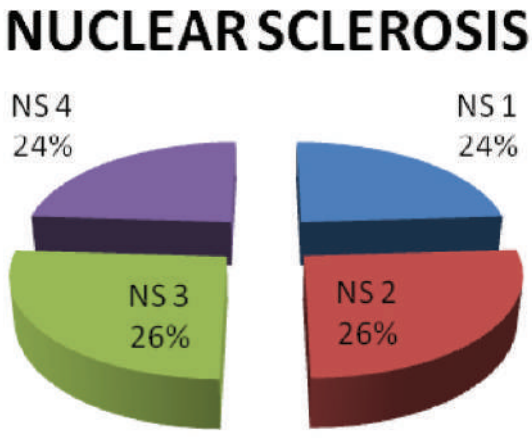


Fig 4. Grades of cataract

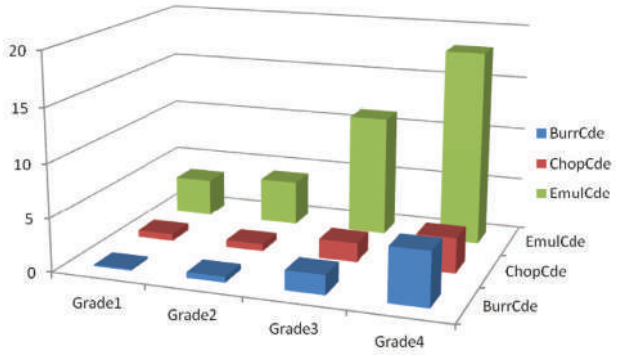


Fig 5.Energy dissipated during different stages

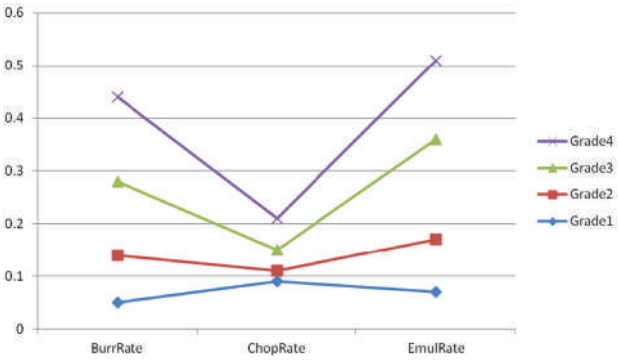


Fig 6. The rate of energy dissipation during different steps of nucleus dissembly

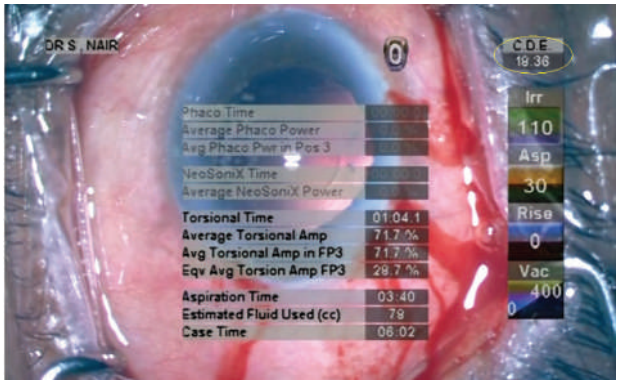


Fig 7.Overview of metrics, top right corner shows cde at any particular time

Cataract Grade	BurrCde	ChopCde	EmulCde	TotalCde	BurrTime	ChopTime	EmulTime	TotalTime
1	0.15	0.65	3.57	4.27	3	6.5	46	55.5
2	0.53	0.67	4.25	5.46	5.5	38.25	43.75	87.5
3	1.81	1.78	11.32	14.88	13	38.33	61.67	108.67
4	4.99	3.28	18.16	26.43	31	57	127.67	215.67

Table 1 Average time and energy for different steps of nucleus dissembly

studied frame to frame, the metrics and time of burrowing ,chopping and emulsification of the nucleus were noted and the values compared for the grade of cataract and the steps of the surgery. This data was analysed using SPSS ver 16.0 software

RESULTS

29 women and 21 men took part in the study.

There were 12 patients with nuclear sclerosis grades 1 and 4, and 13 with grades 2 and 3 respectively.

The average energy used and time taken to deal with the nucleus of each grade of cataract that was recorded is tabulated depending on the step of nucleus management - burrowing, chopping and emulsification.

The energy dissipated showed an increase from burrowing of the phaco tip, through chop and into emulsification. The time taken was also variable so that on plotting the rate of energy dissipation, it was found that it was comparable during burrowing and emulsification but slowed down during chopping.Eg in grade 4 cataract, it was 0.16 for burrowing and 0.15 for emulsification whereas it decreased to 0.06 for chopping.

In grade 1 cataract alone the energy dissipated for chopping was more compared to the other two steps (0.09 for chop versus 0.05 and 0.07)

DISCUSSION

Torsional ultrasound is more efficacious than longitudinal[3,5] owing to the additive effect of the shearing forces of the side to side oscillatory motion of the tip and microcavitation in the former, compounded by the absence of chatter or repulsive forces associated with the latter. Of the various parameters that define efficacy in phacoemulsification including the time taken and postoperative indices, the energy dissipated in the system is the most crucial with regard to post operative results. In the torsional mode ,this is indicated by the cumulative dissipated energy, which is defined as

CDE=TOTAL PHACO ENERGY IN FOOT PEDAL POSITION 3

=TORSIONAL TIME AVERAGE TORSIONAL AMPLITUDE

The factor of 0.4 is applied here as torsional energy is reduced owing to two reasons[2], the frequency of the phaco tip in torsional mode (32 kHz) being 80% of that of conventional phaco (40 kHz), and stroke length of the tip in torsional mode (40 microns) being 50% that in standard mode (80 microns). Reduction in CDE ,therefore implies generation of less energy and intraoperative factors that it depends on, if known , can help control the adverse effects of lens extraction by torsional ultrasound.

Though the apparatus calculates the total CDE[6], we wanted to determine the expenditure of energy in each step of the procedure. The video recordings of these surgeries when analysed frame to frame showed exactly the energy and time taken for a particular step of nucleus management. In this context though the total energy expended for emulsification is more than that for burrowing, so is the time taken for emulsification. To account for this proportional increase in time when we take the rate of energy dissipation into account, they are found to be similar. Chopping ,on the other hand, though utilizing energy takes up a lot of time for intermittent nucleus rotation in between chop, prior to digging in the chopper. These interspersed rotatory movements and time taken for the chop separation are hard to separate from the actual burying of the tip using phaco which is the point of energy generation. This artificial increase in time decreases the rate of energy generation during chop which is reflected in the graph.

Direct chop is a refined technique that can be used for nuclei of any hardness, its advantage being the minimal ultrasound used prior to chopping, unlike divide and conquer or stop and chop. Here the only prechop energy required is to create a small burrow in the central nuclear core for the phaco probe to get enough space for a hold to chop. We utilised this technique, not only because it's a part of our routine procedure but also to use a technique where the prechop energy expenditure is minimum. The prechop and chop energy as a percent of the total CDE for each grade of cataract (table2) shows that 18 to 30 % of the total energy is expended just to break up the nucleus before emulsifying it.

Grade of cataract	Burr + Chop CDE	Total CDE	Percentage
1	0.8	4.27	18.7
2	1.2	5.46	22
3	3.59	14.88	24.1
4	8.27	26.43	31.3

Table 2. Prechop and chop CDE wrt Total energy

The low CDE averages for even higher degrees of nuclear sclerosis[1,7] is an evidence of the efficacy of the system, the technique and the kelman tip subject to surgeon experience.

A corollary of this study would be the derivation that any technology that decreases the energy expended during prechop and chop would be reducing a substantial amount of dissipated energy. The use of laser to fragment

the nucleus is one such procedure that is rapidly gaining ground, and this study validates the advantages of using such a technology.

CONCLUSIONS

Torsional phaco is efficacious in cataract surgeries of even higher grades of nuclear sclerosis as evidenced by the cumulative dissipated energy values. Besides the nuclear grade, energy also depends on the stage of nucleus management, the rate of energy consumption being comparative for nuclear fragmentation and emulsification. Technology decreasing energy consumption during nuclear fragmentation would considerably bring down the CDE.

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Original Article

Correlation Between Preoperative Micro Morphology and Post Operative Anatomical and Functional Outcomes in Macular Hole Surgery

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Abstract

The purpose of the study was to measure the preoperative micro morphological indices (seven indices) in full thickness macular hole measured using spectral domain OCT (SD-OCT) and correlate with postoperative anatomical outcome (Macular hole closure with ultra structural morphology of External Limiting Membrane (ELM) and Inner segment/ Outer segment (IS/OS) junction. Secondary outcome was to correlate the macular hole indices with post-operative functional outcome (Best corrected Visual acuity).

A prospective case series study of 69 eyes of 69 patients. SD-OCT imaging was done for all eyes and macular hole indices were measured. All cases underwent uncomplicated 23G vitrectomy (triamcinolone assisted) with internal limiting membrane (ILM) peeling. SD-OCT images were obtained in the study eyes in follow up mode after 3 months. Anatomical closure, ELM restoration and IS/OS junction layer integrity were studied and correlated with pre-operative indices. Post operative visual acuity was obtained at 3 months and was correlated with all 7 pre-operative macular hole indices. Statistical analysis was done with IBM SPSS Windows V.16.0 Pre-operative micro morphlogical indices in full thickness macular hole measured using spectral domain OCT (SD-OCT) can predict the anatomical and functional outcome of macular hole surgery. Minimum Linear Diameter (MLD) and Base Diameter (BD) were predictive of anatomical closure while Macular Hole Index (MHI) predicted ELM restoration. Post operative visual outcome had significant statistical correlation with Base diameter (BD), Minimum Linear Diameter (MLD), Tractional Hole Index (THI) and Macular Hole Index(MHI)

Introduction

Idiopathic macular holes have received great attention over recent years owing to the improved ability to surgically achieve anatomical closure and regain visual function in many cases.1 Several authors2- 4 have reported significantly higher rates of anatomical closure and visual rehabilitation in patients with stage 2 macular holes compared with larger, stage 3 or 4, macular holes. Optical coherence tomography (OCT) has revolutionized macular imaging and also allows quantitative measurements of many anatomic parameters in vivo

Kusuhara et al in his study showed that Macular hole index (ratio of hole height to base diameter of hole) measured with OCT is a prognostic factor in macular hole surgery5. Laura et al predicted postoperative visual outcome based on hole configuration by optical coherence tomography in eyes with idiopathic macular holes where the macular hole index (MHI) was calculated and correlated with minimum diameter of hole, base diameter of hole, the postoperative decrease in macular thickness, and the postoperative best corrected visual acuity (BCVA)6.

In this study, we have correlated various macular hole indices calculated based on the Spectral domain Optical coherence tomography images with the post operative anatomical and visual outcome.

Purpose

1. To study the preoperative micro morphological indices (seven indices) in full thickness macular hole measured using spectral domain OCT (SD-OCT) namely; Macular Hole Height(MHH), Base Diameter(BD), Minimum Linear Diameter(MLD), Macular Hole Inner Opening(MHIO), Tractional Hole Index(THI), Macular Hole Index(MHI), Hole Form Factor(HFF) and correlate with postoperative anatomical outcome (Macular hole closure with ultra structural morphology of External Limiting Membrane (ELM) and Inner segment/Outer segment (IS/OS) junction)
2. To correlate the macular hole indices with post-operative functional outcome (Best corrected Visual acuity).

Materials and Methods

A prospective case series study of 69 eyes of 69 patients who was diagnosed with full thickness macular hole. All eyes underwent a comprehensive clinical evaluation including presenting best corrected visual acuity, anterior

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segment bio-microscopic examination, direct and indirect fundus examination.

SD-OCT imaging was done for all eyes (Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) in high definition dense scan mode; 20°x20° area with 9 raster B-scans, each composed of 768 A-scans and resulting from an average of 9 frames. The scanning machine has an SD-OCT technology with a confocal scanning laser ophthalmoscope (cSLO). At the baseline examination, each SD-OCT B-scan was registered and saved as a reference image

Macular hole indices were calculated from images (Fig.1)

1. Macular Hole Height(MHH)6 - vertical length between the retinal pigment epithelial layer and the highest portion of the macular hole (fig1.measurement e)
2. Base Diameter(BD)7 – distance measured at the level of retinal pigment epithelium (fig1. measurement a)
3. Minimum Linear Diameter(MLD)8 - minimal extent of the hole (fig1. measurement b)
4. Macular Hole Inner Opening (MHIO)6 – distance between the innermost layer in the macular defect (fig1. measurement f)
5. Tractional Hole Index(THI)9 – e / b (b= MLD)
6. Macular Hole Index(MHI)5 – e / a (b= MLD, a= BD)
7. Hole Form Factor(HFF)7 – c + d / a (c= left arm length, d= right arm length, a= base diameter (fig1.)

All cases underwent uncomplicated 23G vitrectomy (triamcinolone assisted) with internal limiting membrane

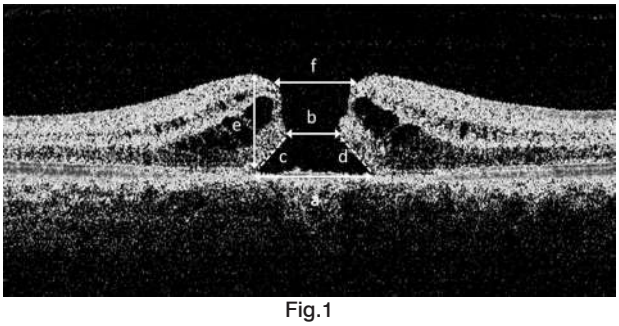


Fig.1

(ILM) peeling. After peripheral truncation of the vitreous base, brilliant blue dye was used to stain the ILM. Once ILM peeling was done across the hole and 360° around the edge of the macular hole. Fluid air exchange was done and gas tamponade by C3F8 or SF6 was performed. All cases were done by a single experienced Vitreo-retinal surgeon. Post operative prone positioning was advised for all cases for 4 days.

SD-OCT images were obtained in the study eyes in follow up mode after 3 months. In the follow up scanning, the eye-tracking system software guided the SD-OCT laser to scan the same location again which was saved in the base line examination. In this way, accurate follow up scan images were obtained and evaluated.

Anatomical closure, ELM restoration and IS/OS junction layer integrity were studied and correlated with pre-operative indices. Post operative visual acuity was obtained at 3 months and was correlated with all 7 pre-operative macular hole indices.

Statistical analysis

Statistical analysis was done with IBM SPSS Windows V.16.0. Independent two sample T test. Mann Whitney test and the association between categorical variables were done with Chi-square test and Fisher exact test.

Results

18(26.8%) were males and 51(73.2%) were females. The mean age was 63.58 +/- 6.24 years.

Table 1. Clinical -Demographic characteristics of study eyes (n=69)

Base line characteristics		Mean± SD (Range)/ Frequency (%)
Gender	Male	18(26.8%)
	Female	51(73.2%)
Age		63.58 ± 6.24 years (51-79 years).
Laterality	Right	36(52.1%)
	Left	33(47.9%)
Lens Changes	Yes	40(57.7%)
	No	20(28.6%)
	IOL	9(12.7%)
Pre operative log MAR		0.94 ± 0.37(0.77-1.77).37204

Macular hole closure or anatomical success was seen in 61 patients (88.4%) and was not in remaining 8 patients (11.6%). Among the 7 pre-operative macular hole indices, 2 were found to have significant association with anatomical success. Minimum Linear Diameter (MLD) (p=0.047) and Base Diameter (BD) (p=0.041) showed statistical significance. (Table 2)

OCT image with measurements.

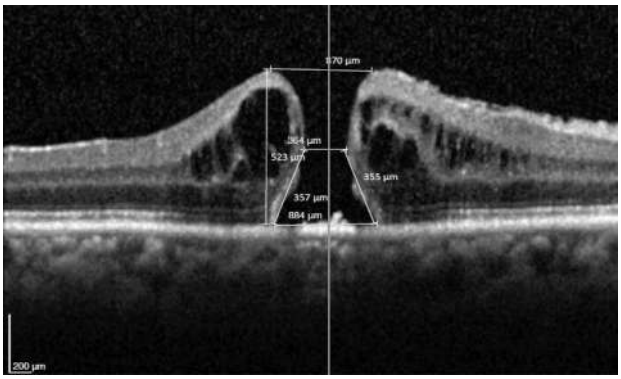


Table 2 Correlation of macular hole indices with anatomical success.

	MH closed (n=61)	MH not closed(n=8)	P value
Macular Hole Height	427.8	459.9	0.45
Base Diameter	832.9	1143	0.047
Minimum Linear Diameter	362.9	541.4	0.041
Macular hole Inner opening	498.5	743.12	0.27
THI	1.96	0.67	0.242
Macular Hole Index(MHI)	0.79	0.48	0.114
Hole form factor(HFF)	12.4	0.68	0.909

The ELM layer was formed in 59 patients (85.5%) & not formed in10 patients (14.5%). The IS/OS layer was not formed in 27 patients (39.13%) & formed in 42 patients (60.86%).

External limiting membrane (ELM) restoration had significant correlation with macular hole index (MHI). It had an inverse correlation with ELM restoration. Restoration of Inner segment-outer segment junction (IS OS) didn't show any significant correlation with the indices.

Table 3. Correlation of Indices with restoration of ELM.

	ELM Formed (n=58)	ELM not formed (n=2)	P value
Macular Hole Height	428.72	469.7	0.42
Base Diameter	821.1	1187.7	0.25
Minimum Linear Diameter	359.4	517.8	0.12
Macular hole Inner opening	497.2	645.5	0.71
THI	1.96	1.12	0.41
Macular Hole Index(MHI)	0.81	0.45	0.05
Hole form factor(HFF)	12.8	0.68	0.91

Functional Outcome

Eyes with anatomical success had a mean pre operative visual outcome was 0.92 ± 0.38 and non closure group was 1.18 ± 0.16. Post-op BCVA at 3 months in the anatomical success group was 0.58 ± 0.32 (p=0.002) and in the non closure group was 0.98± 0.27 (p=0.001) There was a significant improvement in the post op BCVA in both the groups.

Pre operative snellens visual acuity had a negative correlation with functional outcome. Post op BCVA was correlated with all 7 macular hole indices out of which 4 were found to have significant association. Base diameter (BD) (p=0.001) and Minimum Linear Diameter (MLD) (p=0.000) had a positive correlation with the BCVA while Tractional Hole Index (THI) (p=0.03) and Macular Hole Index (MHI) (P=0.007) had statistically significant negative correlation. (table.3)

Table.3
The association between Preoperative micro structural Indices with Postoperative Visual acuity

Factors	Correlation Coefficient	P value
Macular Hole Height	0.206	0.125
Base Diameter	0.443	0.001
Minimum Linear Diameter	0.47	0.000
Macular hole Inner opening	0.17	0.21
THI	-0.29	0.03
Macular Hole Index(MHI)	-0.335	0.007
Hole form factor(HFF)	-0.15	0.251

Discussion

The first study to use OCT to analyse macular holes preoperatively was published by Ip et al[8] in 2002. Continuing on from the original Gass classification,which itself uses biomicroscopic estimation of macular hole size to distinguish stage II from stage III holes, these authors used OCT measurement of the least horizontal diameter of the macular hole to aid classification of the hole into less than 400 μm (stage II) and greater than 400 μm (stage III).

Using a series of logistic regression analyses they found that anatomical closure was associated with macular hole diameters smaller than 400 μm. Given the limitations imposed by OCT resolution at this time, this measurement was the most easily reproducible one. It has been named the MLD or the 'maximum minimum linear dimension' taking into account the need for accurate selection of an OCT image that represents the true extent of the hole. Significant correlations between MLD and visual outcomes after macular hole surgery have been described[10].

The logistic regression analysis done by Laura et al6 in a study indicated that the basic ophthalmic parameters base diameter, macular hole inner opening and MLD are associated with both anatomical and visual success, and exhibit good discrimination with respect to either outcome measure.

In our study, Minimum Linear Diameter (MLD) and Base Diameter (BD) were predictive of anatomical closure. A simple measurement of the distance at the level of retinal pigment epithelium and minimal extent of the hole can predict the chances of anatomical closure of the macular hole. In this study, anatomical success was achieved in 61 eyes (88.4%) with base diameter less than 832.9± 718.9 microns and MLD less than 362.9 ± 221.3 microns. This is comparable to the studies done by Ip et al [8]. The functional outcome is better with lesser MHI and THI. Small holes always show betterment in visual outcome compared to larger holes as calculated by MLD and BD.

This study correlates all the validated pre operative macular hole indices with both anatomical and functional outcome and thereby guiding the vitreo retinal surgeons to choose and give prognostic value for the surgery.

Limitation of the study: Post op visual outcome had post surgery cataract formation as confounding factor. Though excluded with statistical methods, more sample size would have shown more indices to have significant correlation with the functional outcome.

Conclusion

Pre-operative micro morphlogical indices in full thickness macular hole measured using spectral domain OCT (SD-OCT) can predict the anatomical and functional outcome of macular hole surgery. Minimum Linear Diameter (MLD) and Base Diameter (BD) were predictive of anatomical closure while Macular Hole Index (MHI) predicted ELM restoration. Post operative visual outcome had significant statistical correlation with Base diameter (BD), Minimum Linear Diameter (MLD), Tractional Hole Index (THI) and Macular Hole Index(MHI)

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Original Article

Fundus Autofluorescence Imaging in Ocular Toxoplasmosis. Is There Any Role in Monitoring the Inflammation?

Reesha KR DNB, Thomas Cherian MS, Ashok Nataraj MS

Abstract

Purpose: To study the fundus autofluorescence findings in patients with ocular toxoplasmosis at various stages of healing, and also to find out its role in monitoring the inflammation.

Methods: It was a prospective observational case series study involving 21 eyes of 19 patients with ocular toxoplasmosis. Out of the 21 eyes eleven eyes had reactivation of previous toxoplasma retinochoroiditis scar, four eyes had primary retinochoroiditis lesion, two eyes had Toxoplasma neuroretinitis and four eyes had healed retinochoroiditis scar. All patients had undergone standard ophthalmological examination and autofluorescence imaging. Findings observed at presentation and during follow up visits were described.

Results: Eight males and eleven females were included in the study with a mean age of 23yrs. The mean log MAR Visual acuity on presentation was 0.8. All the active lesions were observed as poorly defined area of hyperautofluorescence corresponding to the active retinochoroiditis lesion in fundus imaging (Amorphous pattern). As the lesion healed a well demarcated rim shaped area of hypoautofluorescence was observed surrounding the central hyperautofluorescence by 2-4 weeks (Ring pattern). The hypoautofluorescence was found to be progressing in centripetal fashion, until complete disappearance of the central hyperautofluorescence between six to 20 weeks (Atrophic pattern).

Conclusion: A well defined sequence of changes on fundus autofluorescence was identified in patients with ocular toxoplasmosis at various stages of healing. Findings of the current study suggest that Fundus autofluorescence may be a helpful tool for monitoring the inflammatory process associated with ocular toxoplasmosis.

Introduction

Toxoplasma gondii infection has worldwide distribution, and toxoplasmic retinochoroiditis is the most common form of posterior uveitis in otherwise healthy individuals.[1] Classically, toxoplasmic retinochoroiditis appears as a focus of inner retinitis adjacent to an old chorioretinal scar, and is accompanied by vitritis. During the healing process, the acute lesions resolve, leaving a chorioretinal scar with well-defined hyperpigmented borders and central chorioretinal atrophy. The current study investigates Fundus Autofluorescence (FAF) findings during acute disease and over a 24-week period of follow-up in patients with various clinical forms of active ocular toxoplasmosis.

Patients and methods

A prospective observational case series including patients with biomicroscopic evidence of active ocular toxoplasmosis was designed to evaluate the Fundus Autofluorescence findings during acute disease and their changes over a 24-week period of follow-up. 21 eyes of 19 patients with clinical/serological diagnosis of ocular toxoplasmosis were included in the study. Out of the 21 eyes eleven eyes had reactivation of previous Toxoplasma retinochoroiditis scar, four eyes had primary retinochoroiditis lesion, two eyes had Toxoplasma neuroretinitis and four eyes had healed retinochoroiditis scar. All patients evaluated at the Retina and Uveitis Section of the Department of Ophthalmology, with a diagnosis of active ocular toxoplasmosis between January 2013 and March 2013 were included in the study. The diagnosis was based on the clinical findings, the presence of an active white focal retinal lesion, with or without associated hyperpigmented chorioretinal scars, and confirmed by laboratory studies. All patients had undergone standard ophthalmological examination, fundus imaging and autofluorescence imaging on presentation and during follow up visits. Images were captured with the Carl Zeiss

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FF450 fundus camera with Visupac 4.4. The Carl Zeiss used an exciter filter of 510–580 nm and a barrier filter of 650–735 nm. Lab investigations done in all patients included routine hemogram, Mantoux test and Toxoplasma IgG and IgM antibodies. All patients were treated with combination of sulfamethoxazole (800 mg) and trimethoprim(160mg) orally twice daily for 6 weeks and Azithromycin 500 mg loading dose followed by 250 mg once daily for one month. All patients received prednisolone orally in tapering doses. In cases of Sulpha allergy, treated with Clindamycin 300 mg four times a day for 6 weeks. Patients were reviewed every 2 weeks for two months then every month.

Eight males and eleven females were included in the study. Age group ranged between 12 years to 45 years with a mean age of 23yrs. Out of the nineteen patients two patients had bilateral presentation. The mean log MAR Visual acuity on presentation was 0.8. Four patients had a primary retinochoroiditis patch, of which two patients had macular involvement with initial vision of less than 1[log MAR]. Other two patients had active retinochoroiditis patches involving the superotemporal quadrant. Eleven patients had reactivation of a previous retinochoroiditis scar of which nine were involving the macula. Two patients presented with neuroretinitis with juxtapapillary choroiditis lesion. Two patients had bilateral involvement, with one eye macular scar and other eye reactivation of previous scar. IgG was positive in nine out of twenty patients and IgM was positive only in one patient with a previous scar reactivation. Seventeen patients were treated with Bactrim DS and Azithromycin along with steroids. Two of them had sulpha allergy and were treated with Clindamycin. The mean follow up was 20 weeks.

Three patterns of Fundus autofluorescence patterns were observed.

In a primary active retinochoroiditis lesion, on presentation a poorly defined area of amorphous hyperautofluorescence corresponding to the area of clinically observed lesion was observed (Amorphous pattern). As the lesions healed on follow up between two and seven weeks (median 4 weeks), there was an obvious decrease in the area of amorphous fluorescence encompassing the active retinochoroiditis lesion, and a well defined rim shaped area of hypoautofluorescence observed around the central hyperautofluorescence (Ring pattern). Between 4 and 21 weeeks(median 10 weeks) the rim shaped hypoautofluorescence area was found to be progressing in a centripetal fashion until complete disappearance of the adjacent central hyperautofluorescent region(Atrophic pattern) was noted between 14 and 20 weeks(median 16 weeks) .(Fig:1) In a healed Toxoplasma retinochoroididtis a well defined area of hypoautofluorescence was noted corresponding to the fundus lesion. (Fig 2) In cases of reactivation of previous scar a well defined hypoautofluorescence corresponding to the scar and a poorly defined area of hyperautofluorescence at one edge was noted in the site of reactivation, which became hypoautofluorescent as it healed.(Fig:3) Foveal hypo autofluorescence was associated with decreased visual acuity in 2 eyes.

Discussion

Fundus autofluorescence (FAF) imaging is a noninvasive imaging method which provides additional information not obtainable with other imaging techniques[2], or ordinary fundus examination. Fundus autofluorescence imaging is an in vivo imaging method for metabolic mapping of naturally or pathologically occurring fluorophores of the ocular fundus. The dominant sources are fluorophores such as A2-E in lipofuscin granules that accumulate in the post mitotic retinal pigment epithelium as a by-product of the incomplete degradation of photoreceptor outer segments.[3] Additional in-trinsic fluorophores may occur with disease in the various retinal layers or the subneurosensory space. Minor fluorophores such as collagen and elastin in choroidal blood vessel walls may become visible in the absence or atrophy of RPE cells. Bleaching phenomena and loss of photopigment may result in increased FAF by reduced absorbance of the excitation light. Finally, pathological alterations in the inner retina at the central macula where the FAF signal is usually partially masked by luteal pigment (lutein and zeaxanthin) may result in manifest variations in FAF intensities.

Recording of FAF is relatively easily accomplished, requires little time and is non-invasive. FAF signals are emitted across a broad spectrum ranging from 500 to 800 nm.[3] With the confocal scanning laser ophthalmoscope, excitation is usually induced in the blue range (lambda=488 nm), and an emission filter between 500 and 700 nm is used to detect emission of the autofluorescence signal.[4] Excitation when using the fundus camera is usually done in the green spectrum (535 to 580 nm) and emission is recorded in the yellow-orange spectrum (615 to 715 nm. Because of the difference in excitation and emission spectra, in addition to technical differences between the cSLO and the fundus camera, theoretical considerations would imply that the composition of the detected autofluorescent signal may vary between the systems.

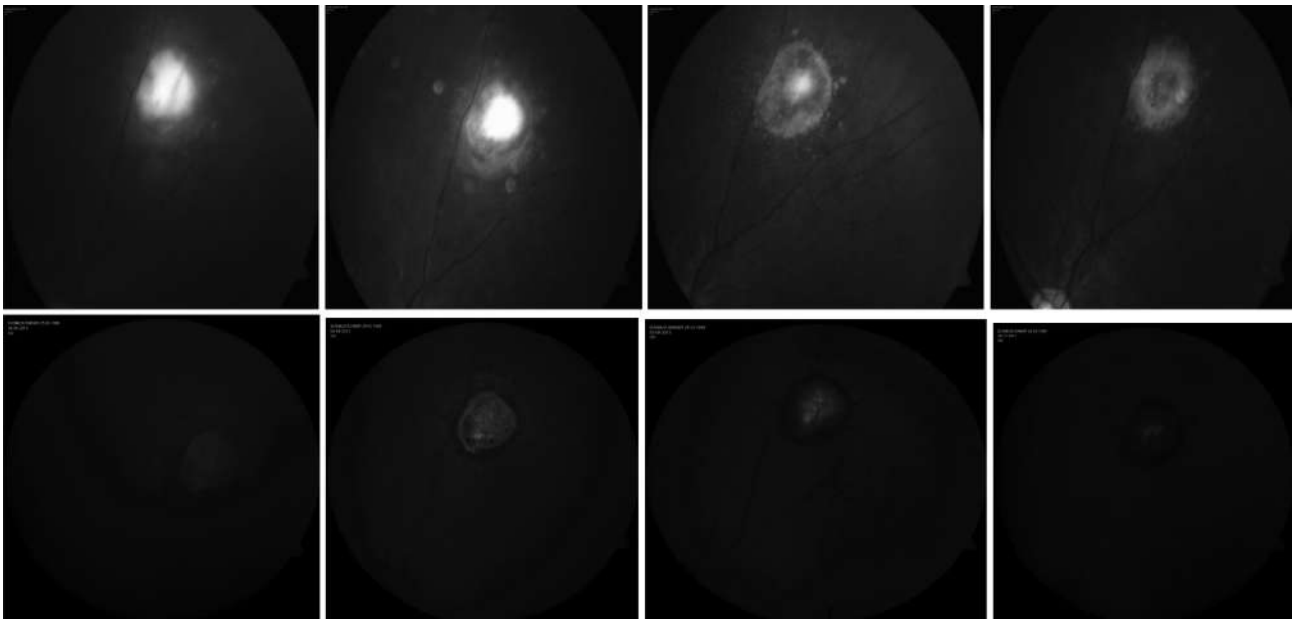


Fig:1- Autofluorescence pattern of healing of a primary active retinochoroiditis

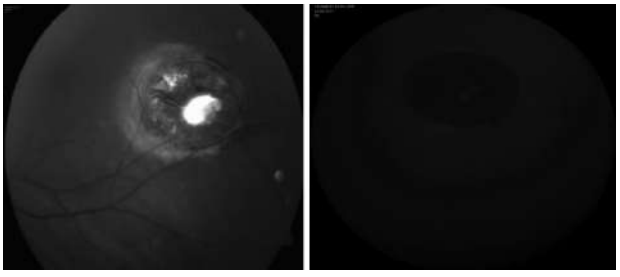


Fig:2 Fundus autofluorescence pattern in Healed retinochoroiditis

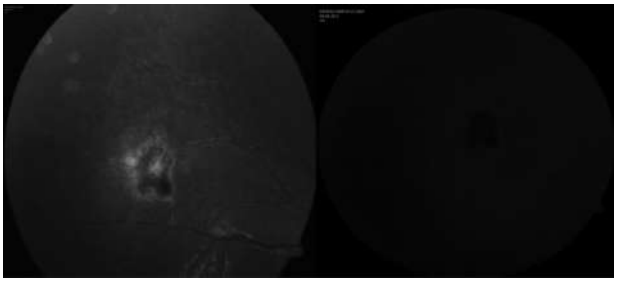


Fig: 3- Autofluorescence pattern in reactivation of a retinochoroiditis scar

The amount of Autofluorescence is determined by the amount of fluorophores, which varies during the acute and resolution phases of inflammation. Hypertrophy and reactive hyperplasia of retinal pigment epithelium (RPE) is associated with increase in AF (hyper autofluorescence), due to accumulation of flurophores. Combination of hyperautofluorescene with hypoautofluorescence pattern was seen in healing retinochoroiditis. Healed lesions appeared as hypoautofluorescence because of RPE atrophy in a retinochoroiditis scar.

Combination of hyperautofluorescence at one edge of a hypoautofluorescent scar was suggestive of reactivation of a Retinochoroiditis scar. Foveal hypo autofluorescence was associated with decreased visual acuity in two eyes.

Conclusion

A well defined sequence of changes on fundus autofluorescence was identified in patients with ocular toxoplasmosis at various stages of healing. Fundus autofluorescence can be used as an additional investigational tool in the diagnosis and management of Ocular Toxoplasmosis. Fundus autofluorescence in eyes with Retinochoroiditis reflects the changes in the outer retinal layers corresponding with the activity of the disease.

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Original Article

Analysis of Bleb Morphology After Trabeculectomy with Anterior Segment Optical Coherence Tomography

Devika.K DO, Girija. K MS, Sindhu. S DO

ABSTRACT

TITLE: Analysis of bleb morphology after trabeculectomy with anterior segment optical coherence tomography.

PURPOSE: To describe the use of Anterior segment optical coherence tomography (AS OCT) in imaging of trabeculectomy bleb to find out the morphology and internal structure, and correlate its internal characteristics with the function of the bleb.

METHODS: Observational case-series study.60 eyes of 53 patient who attended glaucoma OPD during a period of March to May 2013 ,who had previously undergone trabeculectomy Surgery/combined surgery ,with a minimum post operative period of 2 months were included. Bleb morphology clinically noted with slit lamp. Blebs were classified as Filtering (Successful) or Nonfiltering (Failed) depending upon the IOP. Bleb was considered as Filtering bleb if last recorded IOP without any antiglaucoma medication is <18mm Hg if the initial IOP WAS >18mm Hg with or without antiglaucoma medications, 20% reduction in initial IOP if pre operative IOP was <18mmhg without antiglaucoma medications. Blebs were analyzed with Visante AS OCT vertical, horizontal, oblique sections for bleb wall thickness, height of internal fluid-filled cavity,supra scleral fluid space, micro cystic spaces in bleb wall, visible drainage route under the scleral flap.

RESULTS: Images were obtained of 60 blebs. 48 blebs were filtering and 12 were non filtering. The mean preoperative IOP in filtering blebs was 24.31±7.88 mm Hg, and in non filtering blebs were 17.92±6.62 mm Hg. Mean post operative IOP was 11.92± 3.03in filtering and 18.25±6.62 in nonfiltering blebs. % reduction in IOP was 35± 26.24 % in filtering and 6.5±6.76 % in non filtering blebs. AS OCT showed mean bleb wall thickness in filtering blebs is0.70±0.26mm, and in non filtering blebs 0.44±0.24mm.Mean height of internal fluid filled cavity in filtering blebs 0.48±0.29mm, in non filtering blebs is 0.22±0.22m .Supra -scleral fluid space was seen in 43(90%) filtering blebs average size 0.27±0.17mm and only in 5 case of non filtering blebs, average size 0.12±0.20mm. Micro cystic spaces in the bleb wall were present in 33/48 cases of filtering blebs, with an average number being 1.46±1.37 and was present in 2/12 of non filtering blebs, average number of cysts being 0.25±0.62. Route under the scleral flap was present in 44 cases (92%) of filtering blebs and 6 cases (50%) in non filtering blebs.

CONCLUSION: Anterior segment optical coherence tomography (AS OCT) is a promising tool to image trabeculectomy blebs. The different patterns of intra bleb morphology identified by AS OCT were related to the bleb function. The filtering blebs exhibited a large internal fluid filled cavity, thicker bleb walls with more number of micro cysts.

Introduction

Trabeculectomy has been widely applied as treatment of choice in medically uncontrolled glaucoma patients1. The outcome of this surgery depends on the formation of a functioning shunt, termed the filtration bleb, to enable egress of aqueous from the eye. Bleb morphology after trabeculectomy is an important clinical parameter; it is an indicator of bleb function.

A careful slit-lamp examination and colour photography which are non invasive, easy is important in evaluation of bleb function. Two major objective bleb grading systems, including the Indiana Bleb Appearance Grading Scale (IBAGS) and the Moorfields Bleb Grading System (MBGS) have been introduced for clinical evaluation and classification of filtering blebs [2,3] However, bleb evaluation merely based on slit-lamp examination has its own limitations; because of the subjective nature of these methods and the internal morphology of filtering blebs, which could play an important part in determining surgical outcome, cannot be evaluated under slit lamp. Ultrasound biomicroscopy, confocal microscopy, conventional retinal optical coherence tomography (OCT), and time-domain anterior segment AS OCT , are used for analyzing internal bleb characteristics. Ultrasound biomicroscopy and confocal microscopy needs

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direct contact with the eyes, conventional OCT depth of penetration is limited. More recently, anterior segment optical coherence tomography (AS-OCT) has been introduced as a useful imaging device in objective evaluation of filtering blebs[4,5]. AS-OCT provides a high resolution cross-sectional optical imaging of the anterior segment structures via a noninvasive and noncontact procedure, and can provide internal visualization of the blebs.[6,7,8]

Aim of the Study

To describe the use of anterior segment optical coherence tomography (AS OCT) in imaging of trabeculectomy bleb to find out the morphology and internal structure, and correlate its internal characteristics with the function of the bleb.

Material and Methods

This was an observational case series study study of 60 eyes of 53 patients who attended glaucoma OPD during a period of March to May 2013, who had previously undergone trabeculectomy Surgery/combined surgery, with a minimum post operative period of 2 months. Written informed consent was obtained from all patients in accordance with The tenets of Declaration of Helsinki.

Detailed evaluation of all the patients including age, sex, diagnosis and type of glaucoma, pre operative intra ocular pressure, previous antiglaucoma medications, type of surgery performed, post operative period, BCVA, Gonioscopy was done.

Bleb morphology with slit lamp noted in general as diffuse, elevated, flattened.

IOP measured at the time of visit with goldmann applanation tonometry.

Blebs were classified as filtering (successfull) or non-filtering (failed) depending upon the last recorded IOP. Bleb was considered as Filtering bleb if last recorded IOP without any antiglaucoma medication is <18mm Hg if the initial IOP WAS >18mm Hg with or without antiglaucoma medications, 20% reduction in initial IOP if pre operative IOP was <18mmhg without antiglaucoma medications.

The Bleb was then imaged using a prototype of the Visante Anterior Segment –Optical Coherence Tomography (AS OCT) (Carl Zeiss Meditec Inc). The subject was asked to look down and the upper Lid gently retracted to expose the bleb as fully as possible in the Superior bulbar conjunctiva, taking care to avoid pressure on the Globe or bleb. Standard AS-OCT images were obtained for each Bleb with horizontal,vertical and oblique sections in high resolution corneal mode and the best section was used for analysis.

Blebs were analyzed in terms of quantitative as well as qualitative parameters. Quantitative parameters like maximum and minimum bleb wall thickness above the fluid-filled cavity, and the maximum height of the internal fluid-filled cavity, presence or absence of micro cysts ,and number of micro cysts in the bleb wall, supra-scleral fluid space. Qualitative parameters, includes the visibility of the drainage route under scleral flap and bleb wall reflectivity. All measurements ,from the best possible sections were performed by the single operator.

Bleb wall thickness is defined as the distance between the first reflective signal from the conjunctiva to the top of the sub-conjunctival fluid space, As bleb wall thickness may vary along the scan, only the minimum distance was measured. The internal fluid-filled cavity was defined as a significantly low-reflective fluid-filled space adjunct to the scleral flap in millimeters , measured on the horizontal scans . Or the maximal thickness of the signal void or hyporeflective area directly beneath the bleb wall in the cross sectional image. The suprascleral fluid space was measured as the maximal vertical distance in the signal void area adjacent to the sclera.Internal reflectivity was classified as high if the reflectivity of internal structures of filtering bleb was similar to sclera,and low if the reflectivity was less than sclera.

Results

Images were obtained of 60 blebs . There were 20 (33.3%) Males and 40 (66.7%)females with a mean age of 65.13±8.87 Years. 48 were filtering and 12 were non filtering. Of 60 eyes, 41 had primary open-angle glaucoma, 14 had primary angle-closure glaucoma, and 4 pseudoexfoliation glaucoma, 1 had pigmentary glaucoma. 45 eyes had combined surgery, 8 had trabeculectomy and 7 had augmented surgery with Mitomycin C of which one was combined and 6 were trabeculectomy.. The mean duration from the time of Trabeculectomy surgery to the AS OCT examination ranged from 2 months to 60 months.

Analysis done using SPSS 20 version.

Since the data is non-normal Man-Whitney test is used for analysis,

The mean preoperative IOP in filtering blebs was 24.31±7.88 mm Hg, and in non filtering blebs were 17.92±6.62 mm Hg. Mean post operative IOP was 11.92± 3.03in filtering and 18.25±6.62 in non filtering blebs. % reduction in IOP was 35± 26.24 %in filtering blebs and 6.5±6.76 % in non filtering blebs.

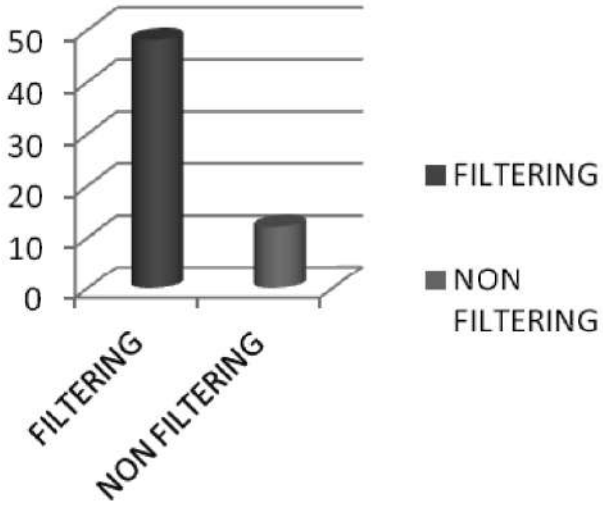


Figure 1:shows the outcome of surgery

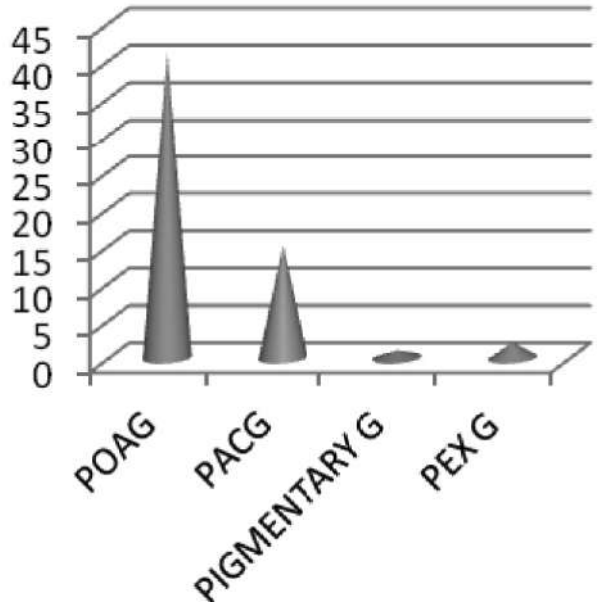


Figure 2: shows the pre-operative diagnosis

AS OCT showed mean bleb wall thickness in filtering blebs is0.70±0.26mm, and in non filtering blebs 0.44±0.24mm. .Mean height of internal fluid filled cavity in filtering blebs 0.48±0.29mm in, non filtering blebs is 0.22±0.22mm. Supra scleral fluid space was seen in 43(90%) filtering blebs average size 0.27±0.17mm and only in 5 cases of non filtering blebs, average size 0.12±0.20m.

Micro cystic spaces in the bleb wall was present in 33/48 cases of filtering blebs, with an average number being 1.46± 1.37 and was present in 2/12 of non filtering blebs, average number of cysts being 0.25±0.62.Route under the sclera flap was present in 44 cases (92%) of filtering blebs and 6 cases (50%) in non filtering blebs. The 36/44 (81 %) of OAG become filtering and (13/16) 81.25% of ACG become filtering.

In our study we concluded that there is no significance in outcome between male or female, between primary open angles or primary closed angle glaucoma, and whether the surgery was combined, trabeculectomy, or augmented surgery with MMC. But the average bleb wall thickness, height of internal fluid filled cavity, number of cystic spaces and suprascleral fluid space was higher in ACG compared to OAG.

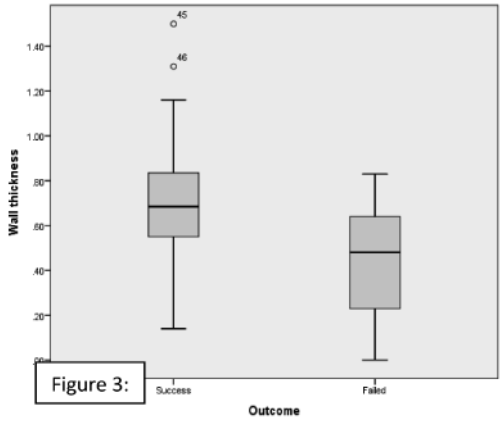


Figure 3: BOX PLOT SHOWING THE BLEB WALL THICKNESS IN FILTERING AND NON-FILTERING BLEBS:

Variable	Filtering bleb	Non-filtering	P value	
Pre-operative IOP	24.31±7.98	17.92±7.23	0.009	Significant
Post-operative IOP	11.92±3.03	18.25±6.62	0.001	Significant
% Reduction in IOP	35.20±26.24	6.5±6.76	0.001	Significant
Bleb Wall thickness	0.70±0.26	0.44±0.29	0.009	Significant
Height of Int. fluid cavity	0.48±0.29	0.22±0.22	0.002	Significant
Number of Cystic spaces	1.46±1.37	0.25±0.62	0.002	Significant
Supra scleral fluid space	0.27±0.17	0.12±0.20	0.002	Significant

Table: 1 shows the various parameters measured in filtering and non-filtering blebs

It has been found that the mean pre op IOP in patients underwent augmented surgery was 32.57±5.86mm Hg and with a mean reduction in IOP 46.19±34.47 %, all were filtering blebs .Out of successful blebs 5 were clinically flat. Of Failed blebs 7 were flat, 2 were clinically diffuse,3 were elevated. In elevated blebs one had iris blocking the trabeculectomy ostium, and the bleb wall intensity was high in all blebs. 2 were considered as encysted blebs.

Discussion

Anterior segment optical coherence tomography was useful in showing cross-sectional images of internal bleb structure that were previously inferred from clinical examination. OCT offers a better alternative for bleb imaging compared with UBM, OCT also provides higher axial resolution images (18 mm in Visante versus 25 mm in UBM) translate into more accurate and reproducible images for direct and objective bleb assessment and measurement.

In this study we observed that bleb wall thickness above the fluid-filled cavity, the maximum height of the internal fluid-filled cavity, presence or absence of micro cysts, and number of micro cysts in the bleb wall, supra-scleral fluid space, visibility of the drainage route under scleral flap and bleb wall reflectivity are good indicators of bleb function.

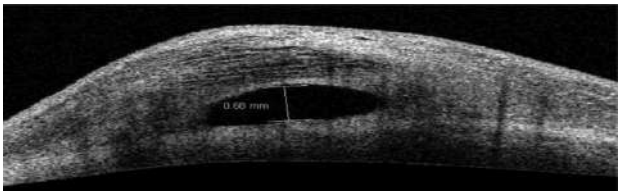


FIGURE 4: Diffuse filtering bleb ,thick hypo reflective bleb wall, good fluid cavity

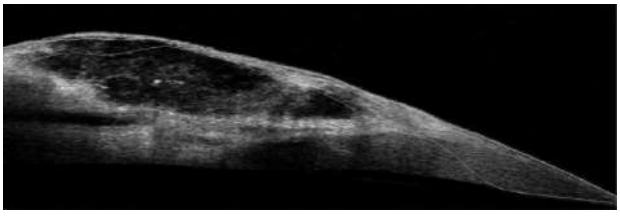


FIGURE 5: Cystic, Elevated bleb,thin wall with large fluid filled cavity

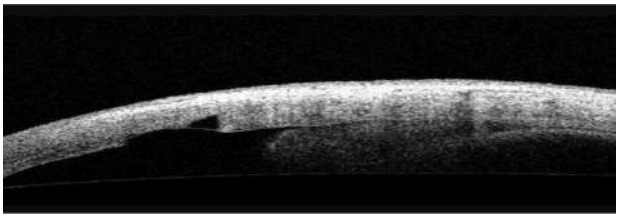


FIGURE 6: Flat bleb,non filtering, hyper echoeic wall.

Filtering blebs were characterized by thick bleb wall with micro cysts on the bleb wall, with fluid filled cavity beneath the bleb and presence of suprascleral fluid space and visible drainage route under sclera flap and low reflectivity in the bleb wall. These findings were similar to the results of study done by Keisuke Kawana et al.[10] Filtering elevated cystic blebs were having large and multiple micro cysts on the bleb wall, with reduced wall thickness and large fluid filled area underneath. The thinner conjunctival wall in cystic blebs explains why these blebs are more prone to complications. Most of the filtering blebs were clinically diffuse.[11] Filtering blebs which were clinically flat, on AS OCT shows average bleb wall thickness 0.51mm, height of internal fluid cavity 0.67mm. Previous studies using AS OCT by Leung CK et al and mandeep singh et al also have demonstrated that successful blebs have thicker walls[4,5]

Non filtering blebs in general were characterized by low bleb wall thickness, small or absent internal fluid space, well apposed sclera flap characterized by absence of visible route under sclera flap,low or absent supra sclera fluid space,highly reflective bleb walls. In our study ,of 12 non-filtering blebs blebs 7 were clinically flat, 2 were clinically diffuse,3 were elevated. In elevated failed blebs one had got iris blocking the trabeculectomy ostium, and the bleb wall intensity was high in all blebs. These two were considered as encysted blebs.

Imaging of the flap and ostium in the early post op period by AS-OCT may be of importance in guiding early intervention to optimize aqueous flow through the bleb. For example, laser suturelysis /release of suture is indicated in the case of a tightly apposed scleral flap[7,9]

There are a number of limitations using Visante OCT for bleb imaging. Visante OCT the software is primarily designed to image and measure anterior chamber structures. Therefore, measurements made on the bleb images may not reflect true values. Another limitation is that Visante OCT does not provide signal intensity measurements. The grading of intrableb reflectivity is essentially a subjective. This was a observational study and measurements were performed at different time points after trabeculectomy. A prospective study evaluating the time course of changes in the bleb morphologic features is required.

Conclusion

Anterior segment optical coherence tomography (AS OCT) is a promising tool to image trabeculectomy blebs.It was able to demonstrate features of bleb which is not visible in slit lamp.The different patterns of intra bleb morphology

identified by AS OCT were related to the bleb function. Combining both clinical and imaging information could provide a new perspective towards understand the different surgical outcomes after trabeculectomy. The filtering blebs exhibitted a large internal fluid filled cavity,thicker hyporeflective bleb walls with more number of micro cysts and a visible route under sclera flap.

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Original Article

Anterior Segment Optical Coherence Tomography (AS-OCT) and Ultrasound Biomicroscopy (UBM) in Detecting Plateau Iris Configuration (PIC) in Patients with Narrow Angles

Dipali Tanajirao Chavan DNB Trainee, Meena Nair MS, FGO, Thomas George MS, K G R Nair MS, FRCS

ABSTRACT

Purpose: To evaluate the utility of ASOCT (Spectralis) and UBM (Ellex) in patients with angle closure to detect plateau iris configuration.

Methods: This is a prospective cross-sectional observational study done at our glaucoma clinic, between January - April 2013.30 eyes of 15 patients with appositional or synechial closure were enrolled. Gonioscopy was done to identify PIC by sine wave sign. All patients underwent imaging using ASOCT and UBM to detect PIC.ASOCT focused on iris profile and iridoangle variations.UBM defined Plateau iris in a quadrant as anteriorly directed ciliary processes, absent ciliary sulcus ,steep iris root from its insertion point, flat central iris plane and iridoangle contact. At least two quadrants had to fulfill this criteria.

Result: Of 30 eyes, PIC was identified in 10 eyes by Gonioscopy , 8 eyes by ASOCT, 10 eyes by UBM. ASOCT and UBM showed a fair agreement in 8 eyes. One patient (2eyes) had apposed peripheral iris hence steep iris was not demonstrated by ASOCT but seen by UBM. Only 2 eyes were confirmed as PIC by all three modalities. 60% eyes had the gonioscopic PIC feature due to thick peripheral iris roll and one patient detected by gonioscopy had absent ciliary processes rotation in UBM. Synechial closure, ciliary body cyst were other causes for an absent sine wave sign.

Conclusion: Gonioscopy is still a good screening tool to identify PIC. Imaging devices (UBM and ASOCT) have complementary role in the diagnosis of PIC, but never interpret images in isolation.

INTRODUCTION

Primary angle closure glaucoma (PACG) is a major cause of visual morbidity of glaucoma in East Asia.[1,2] Recent evidence has shown that non pupil block mechanisms such as plateau iris may play far more important role in the PACG disease process than previously thought[3].

Plateau iris has been traditionally defined as an occludable angle on gonioscopy with a flat iris plane and relatively deeper central anterior chamber[4]. The advent of imaging tools as UBM and ASOCT have helped to increase the understanding of plateau iris.

Hence the aim of our study is to evaluate the utility of ASOCT (Spectralis) and UBM (Ellex) in patients with angle closure to detect plateau iris configuration .we have also attempted to compare the above imaging tools with conventional gonioscopy in our screened study group.

MATERIAL AND METHODS

This is a prospective cross sectional observational study done at our glaucoma clinic during the period of January to April 2013.

A thorough history, visual acuity with refraction followed by a detailed slit lamp biomicroscopic examination of the anterior segment was routinely done on all patients attending the glaucoma clinic of a single consultant of a tertiary eye care centre. A complete ophthalmic evaluation was done which included both a central and peripheral anterior chamber depth grading by Van Herrick's test to identify patients with narrow angles (< grade 2).After intraocular pressure assessment by Goldmann applanation tonometry, gonioscopy was performed by a single examiner in low ambient light using a Goldmann 2 mirror goniodiagnostic lens at 16 x magnification with the eyes in the primary position. A narrow angle was defined as Shaffer grade < /= 2 in three or more quadrants . Indentation gonioscopy was performed with a short and narrow beam width of the minimum possible illumination was done with a Sussmann 4 mirror gonioprism to confirm occludable angles and make a note on appositional or synechial closure and to identify the typical sine shaped curve of the iris surface called "sine wave sign" or the "double hump sign" which is an accepted indicator of PIC. Thus all patients with appositional or synechial closure were enrolled in the study which included

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15 patients(30 eyes).

Eyes that had a history of intra ocular surgery or laser iridotomy or iridoplasty , opaque cornea were excluded. Following gonioscopy ,all the enrolled subjects underwent anterior segment imaging with Anterior Segment Optical Coherence Tomography (ASOCT) and Ultrabiomicroscopy scan (UBM) evaluation to identify plateau iris configuration . ASOCT (Spectralis – anterior segment module @ Heidelberg engineering GMbh) was performed with the participants in the sitting position fixating on an internal target with focus adjusted with reference to the subject's refractive error at distance in dim ambient light .Images of superior ,inferior ,nasal and temporal angle quadrants were captured by a single examiner. Three images taken for each eye and best quality of image was selected for a qualitative analysis of the iris profile and iridoangle variations . The configuration both central and at the level of iris root to identify PIC and appositional or synechial extent was noted.

After ASOCT evaluation UBM was done using a 50 MHz transducer. The parameters of the UBM (Ellex Eye cubed version 4 system, Ellex Medical pty ltd, Australia) were set at 80 db ,5 db gain compensation ,approximately50 μm resolution and was done by a single examiner masked to the other test results, under standardized conditions to control accommodation and room illumination. Direction of gaze was standardized by placing a marker on the ceiling to optimize variations of the eye .Each patient was examined after instilling 0.5% proparacaine drops in the supine position .3,6,9 and 12 o'clock positions of the angles were scanned. Scanning was performed until the scleral spur and ciliary processes were clearly imaged. Probe was held perpendicular to the ocular surface and attempts were made to prevent the eyecup from compressing the globe and thus causing changes to the angle configuration.

UBM defined plateau iris in a quadrant as anteriorly directed ciliary process, absent ciliary sulcus, steep iris root from its insertion point, flat central iris plane and irido-angle contact. In UBM imaging above criteria had to be fullfield in at least two quadrants to diagnose a patient as plateau iris[5]

Cases detected to have a plateau iris configuration by gonioscopy , ASOCT and UBM were charted and the results obtained from the imaging modalities were compared with conventional gonioscopy to analyse the cause for a disparity if present in a case. Statistical analysis was performed to assess the agreement between the imaging modalities using kappa numeric rating . (statistical software – SAS 9)

Result

15 (30 eyes) individuals were enrolled in our study which comprised of 6 males and 9 females. Our patients were in the age group of 38-80 years. (Mean Age 56 years)

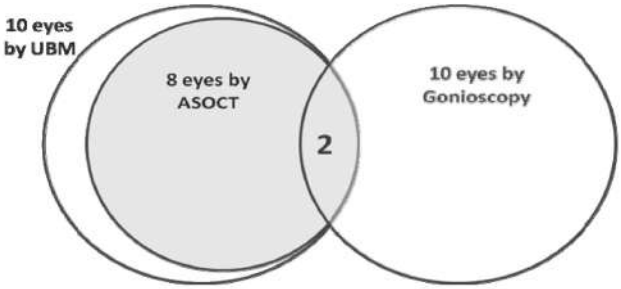
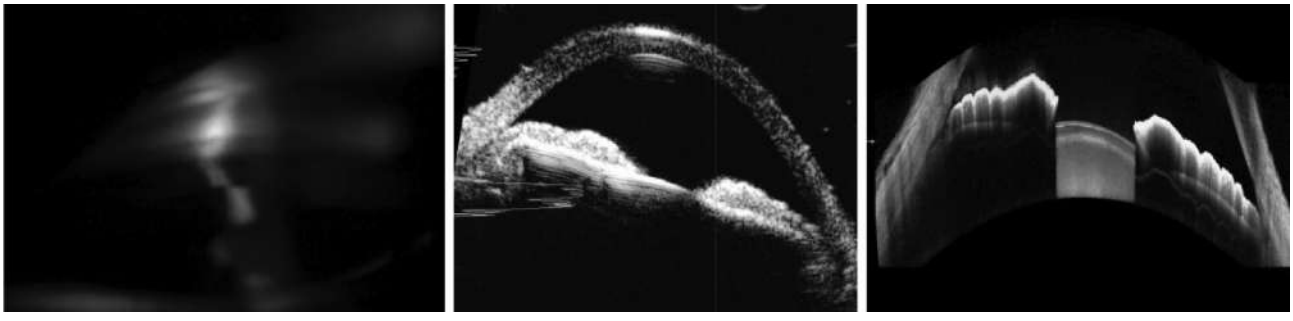


FIGURE- 2 : Gonioscopy versus ASOCT versus UBM in PIC detection

Out of 18 eyes detected as PIC ,10 eyes identified by gonioscopy, 10 eyes by UBM and 8 eyes by ASOCT
2 eyes were detected by all 3 methods

	PIC identified by		
Method used	Gonioscopy	ASOCT	UBM
Gonioscopy	10	2	2
ASOCT	2	8	8
UBM	2	8	10

TABLE – 1: Statistical analysis showing agreement between ASOCT and UBM in detection of PIC.



(A) (B) (C)

FIGURE – 1 - PIC identified by (A) gonioscopy (B) UBM (C) ASOCT

kappa for, UBM vs ASOCT = .781 (.0003) Substantial agreement

Interdevice (ASOCT and UBM) agreement in evaluating detection of PIC as measured using kappa statistic shows value of 0.781 (0.0003) considered as a substantial agreement.

< 0 - Less than chance agreement , 0.01–0.20 -Slight agreement , 0.21– 0.40-Fair agreement 0.41–0.60 -Moderate agreement ,0.61–0.80 -Substantial agreement, 0.81–0.99 -Almost perfect agreement.

MASTER CHART

Sr no	MR No	GO-NIOS-COPY	AS-OCT	U B M	DIAGNOSIS / EXPLANATION (in relation to gonioscopy interpretation)
1	297701	Y	Y	Y	Plateau iris
2	297701	Y	Y	Y	Plateau iris
3	396721	N	Y	Y	PAS ,B/L ciliary body cyst
4	396721	N	Y	Y	PAS, b/l ciliary body cyst
5	371103	N	N	Y	PAS
6	371103	N	N	Y	PAS
7	324256	Y	N	N	PTIR
8	324256	Y	N	N	PTIR
9	395675	Y	N	N	PTIR
10	395675	Y	N	N	PTIR
11	394444	Y	N	N	PTIR
12	394444	Y	N	N	PTIR
13	389399	N	Y	Y	PAS
14	389399	N	Y	Y	PAS
15	396461	N	Y	Y	PAS
16	396461	N	Y	Y	PAS
17	397215	Y	N	N	absent ciliary process rotation demon-strated
18	397215	Y	N	N	absent ciliary process rotation demon-strated

TABLE -2 showing details of each patient identified as PIC by gonioscopy/ ASOCT/ UBM.

PAS =Peripheral anterior synechiae , PTIR = peripheral thick iris roll Gonioscopy , ASOCT ,UBM in PIC detection :Yes (Y)/No (N)

Out of 30 eyes screened only 10 eyes were detected as

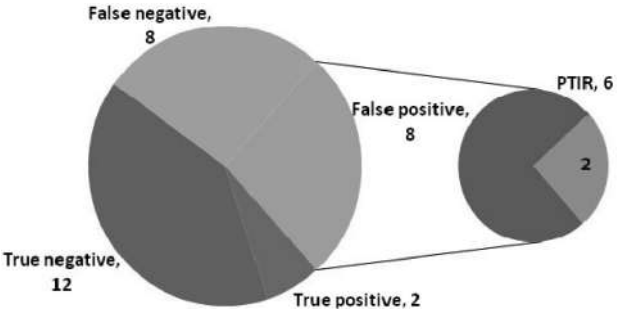


FIGURE 3 : Analysis of study group (30 eyes)detected as PIC by gonioscopy. (To refer next page for explanation)

PIC by gonioscopy (positive sine wave sign). Of it, only 2 eyes were true positive (as confirmed with the imaging modalities). Remaining 8 eyes did not correlate with imaging devices, hence were false positive, the cause analysed mainly due to thick peripheral iris roll (6 eyes) and 2 eyes had a wide ciliary sulcus in UBM ,hence was not a typical plateau iris. False negative in gonioscopy results to those who did not show the sine wave sign, major cause being synechial angle closure. True negative refers to those who were not plateau iris by all these diagnostic modalities.

Discussion

Plateau iris was first described in 19587 by Tornquist.PIC is defined as a narrow or closed iridotrabecular angle associated with a flat iris plane and relatively normal anterior chamber depth. It is the anatomic appearance whereby the iris root from its insertion point at the iridocorneal angle initially angulates sharply forward and then curves centrally to reveal the characteristic double hump appearance also called 'sine wave sign' in indentation gonioscopy. Indentation presses the iris surface backward ,the deepest point of indentation is not at the iris periphery but at approximately two-thirds of the distance between the centre of the pupil and the iris root, the iris rises again from this point to the site of appositional closure. A "double hump sign" observed on indentation gonioscopy is strongly correlated with the presence of a plateau iris(Kiuchi et al ;2009,Ritch 1992).[8]

PIC is caused by anteriorly located ciliary processes which close the ciliary sulcus and provide support to the peripheral iris. UBM provides us with a method of examining the anterior segment of the eye in depth at high resolution. The advent of ASOCT in 1994 further made available a non contact technology for axial and lateral resolution of anterior segment imaging and with a limited depth of penetration of 3-6 mm depending on scan type.

Our study screened the same study group with the two imaging modalities to determine the agreement and compared it with typical gonioscopic findings to assess the relative strengths and weaknesses of different methods in the detection of a plateau iris configuration.

In our series of 30 eyes identified as narrow angles and enrolled in the study group, 18 eyes were detected to have a PIC. Of them, 10 were identified by gonioscopy, 8 by ASOCT and 10 by UBM. Only two eyes were identified as a PIC by all the three modalities. All the 8 eyes detected by ASOCT were rather confirmed by UBM as shown by the substantial agreement of 0.78 rating by Kappa statistical analysis6.UBM in addition identified a patient as PIC not detected by gonioscopy and ASOCT on account of absence of typical iris contour changes due to synechial angle closure. UBM further demonstrated the absence of anterior rotation of ciliary processes in case of plateau iris detected by gonioscopy. A case of bilateral ciliary body cyst which caused elevation of iris leading to a pseudoplateau configuration was detected by UBM imaging technique. The sine wave sign was absent in this patient in gonioscopy due to broad focal peripheral anterior synecchiae. A UBM study conducted by Kunimatsu.S et al showed that cysts were detected in 54.3% of their study group and Tarichara et al reported pseudoplateau iris with bilateral iridociliary cysts.

UBM is thus a very useful imaging tool in the diagnosis of plateau iris because it can visualize structures posterior to the iris like the ciliary body that are otherwise not visible by clinical examination methods like gonioscopy.[6]

In our patient series, 60% of the double hump appearance (pseudo PIC) in gonioscopy was due to a thick peripheral iris roll. This has been reported as the most common cause of a differential diagnostic confusion of plateau iris in Roy and Fraunfelder's current ocular therapy[7]. Synecchial angle closure in our study is the major cause for the negative sine wave sign in gonioscopy in the cases detected as PIC by the imaging modalities.

Gonioscopy remains the reference standard in identification of angle closure disease and is definitely a basic tool to diagnose plateau iris configuration in expert hands though subjective[4]. However the confounding factors should be kept in mind during interpretation and if there is a facility for UBM imaging of the angle, definitely the reproducibility and confirmation of diagnosis will be higher.

Limitations of our study include the small sample size since only the patients attending a single consultant's Pclinic during the study period have been enrolled. Variability in UBM and ASOCT findings due to the imaging techniques.

Conclusion

Both OCT and UBM showed excellent performance in identifying eyes with plateau iris.ASOCT is a rapid , non contact imaging modality and can detect indirect sign of plateau iris in a sitting patient.UBM confirms the plateau iris by showing the iris root indentation cause by cilliary body. Gonioscopy however is a good screening tool to identify plateau iris configuration if one is experienced in indentation gonioscopy.

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Original Article

A Step Ahead in Understanding Central Serous Chorioretinopathy Using Spectral Domain Optical Coherence Tomography

Dr. Eliza Anthony DNB, Dr. Mahesh G MS, FRCS, Dr. A Giridhar MS

ABSTRACT

Purpose: To describe the ultrastructural changes of the retinal pigment epithelium (RPE) at the fluorescein leakage site and other micromorphological alterations in central serous chorioretinopathy (CSCR) using spectral domain optical coherence tomography (SDOCT) and to correlate these tomographic changes with best corrected visual acuity (BCVA).

Methods: Prospective case series of 53 eyes of 50 consecutive CSCR patients undertaken over a period of 6 months. All patients underwent complete ophthalmological examination, SDOCT (Spectralis, Heidelberg, Germany) and fluorescein angiography (FFA). According to chronicity and recurrence patients were divided into 4 categories A, B, C and D. Morphology of RPE at leakage site, pigment epithelial detachments (PED), serous macular detachment (SMD), outer nuclear layer thickness(ONLT), highly reflective dots, fibrin and other alterations were recorded and correlated with BCVA. Bridge was defined as sagging of posterior neurosensory retina. Analysis was done using SPSS V16 software.

Results: Subfoveal SMD height and ONLT showed significant correlation with BCVA ($P<0.05$). Commonest PED location was underlying SMD in all categories. Commonest type of PED was dome shaped in all categories except category C where low to flat PED was common. Among 27 leakage site, micro rip, protrusion and irregular RPE was seen in 12(44.4%), 13(48.1%) and 2(7.4%) sites respectively. Commonest leakage site morphology was RPE protrusion in category A,C,D and micro rip in category B. Hyperreflective dots and bridge were seen in 43(81.1%) and 11(20.8%) symptomatic eyes respectively. ONLT was significantly decreased in symptomatic eyes ($P = 0.000$).

Conclusion: Detailed morphological examination using SDOCT helps to understand pathological mechanism of CSCR and to identify the RPE abnormalities at leakage point which can aid in focal laser treatment in CSCR patients. Decrease in ONLT can help to prognosticate the visual acuity in CSCR patients.

Introduction

CSCR is serous detachment of the posterior pole that typically affects young and middle aged adults.[1] The primary pathology is thought to be hyperpermeability of choroid, possibly as a result of stasis, ischaemia, or inflammation.[2] Hyperpermeable choroidal vessels are thought to increase the tissue hydrostatic pressure which promotes formation of RPE detachments (PEDs), overwhelms the barrier function of the RPE, and allows exudation from the choroidal vasculature to pass into the subretinal space. This hypothesis is based on FFA and indocyanin angiography (ICG) findings which demonstrates choriodal staining in the mid phase of ICG angiography which is usually contiguous with the foci of RPE leakage seen on FFA.[3,4,5] However, invasive modalities like FFA and ICG do not provide enough information about changes at RPE level and in different layers of retina.[6]

Fundus autofluorescence(FAF) is a simple noninvasive method to assess the metabolic activity of RPE.[7] Focal leakage at the level of RPE in FFA, is seen as a hypoautofluorescent spot on FAF. However, FAF does not provide anatomical details of RPE and outer retina.[8]

SDOCT is an advanced noninvasive imaging modality that reduces the scan acquisition time and enables to image in detail the anatomical changes in eyes with CSCR and thus plays a very important role in diagnosis, treatment and follow up of CSCR patients especially when invasive test could not be performed. Many studies have described the detailed morphologic changes that occur in the RPE and the outer retina, including serous retinal detachment (SRD), RPE abnormalities such as PED, small RPE protrusions, focal defects in the RPE monolayer at the leaking site, fibrinous exudates in the subretinal space, and subretinal precipitates.[9]

Acute CSCR usually has a self limiting course, where as chronic CSCR with sustained sub retinal detachment (SRD) may need active intervention such as photodyanamic

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therapy (PDT), to prevent permanent visual disturbance.9 Therefore determination of chronicity of disease is important for making an appropriate treatment choice and for predicting the prognosis.

In this study we have described the precise morphological changes that occur in inner and outer retina especially RPE layer at the leakage site, their correlation with visual acuity and the duration of the disease which aid in better understanding of the mechanism of CSCR, especially the abnormalities in the RPE layer.

Aim of Study

To describe the ultrastructural changes of the retinal pigment epithelium (RPE) at the fluorescein leakage site and other micro morphological alterations in central serous chorioretinopathy (CSCR) using spectral domain optical coherence tomography (SDOCT) and to correlate these tomographic changes with best corrected visual acuity (BCVA).

Materials and Methods

A prospective case series of 53 eyes of 50 consecutive CSCR patients was undertaken over a period of 6 months from August 2012 till January 2012. This study had approval by institutional ethical and scientific committee. According to chronicity and recurrence patients were divided into 4 categories. CSCR patients for whom the onset of symptoms such as visual loss, metamorphopsia, chromatopsia, or micropsia had occurred less than 1 month before presentation were category A; symptom onset between 1 month to 3 months were category B and symptomatic for more than 3 months were category C. If the patient had any previous episode discovered during subjective recollection or the review of medical records were defined as recurrent and were included in category D.

Diagnostic criteria: CSCR was diagnosed as either classic form, a circumscribed area of serous detachment of the neurosensory layer of retina with or without PED in the macular region associated with solitary or few leaks seen in FFA, or a diffuse retinal pigment epitheliopathy which was indicated by a widespread area of RPE changes associated with many angiographic leaks.

Exclusion criteria: Eyes with polypoidal choroidal vasculopathy, age related macular degeneration and any other inflammatory pathology that could compromise visual acuity and with history of previous photodynamic therapy or intravitreal injection of anti-vascular endothelial growth factor were excluded.

Measurement method: All patients underwent complete ophthalmological examination, SDOCT (Heidelberg Engineering, Heidelberg, Germany) and FFA. The light source of SDOCT is a super luminescent diode of average wavelength 870nm. It uses an ultra high scan speed of 40,000 Ascans per second. Both eyes were dilated and line scans comprising 16 frames equally spread in a rectangular area of 8.6 x 7.2 x 1.9 mm (lateral x lateral x depth) were taken in both eyes in central 30^{o} of macula. 61 B-scans were acquired and each B-scan is 768 A scans per frame. The distance between each B scan was 120μ and the scan acquisition time was 35 seconds. The measurements were performed by 2 examiners independently using the caliper measurement tool in the SDOCT system. If the difference between the 2 examiners was >15% of the mean of 2 values, then there was open adjunction with the senior author.

Subfoveal and maximum height of SMD (fig1) was obtained by measuring distance between the outer border of sensory retina and the inner border of the RPE at the central fovea and at the highest point of SMD respectively. Width of SMD was measured as the extent of SMD. Absence and presence of PED was recorded. PED was classified into 2 types: dome shaped PED which had a typical semicircular pattern and a flat PED which had an irregular low to flat pattern. On the basis of location, PED was classified as one underlying SMD and the other present elsewhere. RPE protrusion was defined as RPE bumps in the absence of optically empty space beneath the RPE. Irregular RPE was seen as irregular thickening of the RPE. Focal RPE defect within the PED at the leakage site was defined only when high OCT signal was seen in the choroidal layer posterior to the defect for preventing confusion from posterior shadowing effect by dense structures such as blood vessels. To detect RPE changes corresponding to the leakage sites, SDOCT images were minutely observed at the site corresponding to the FFA leak. Changes at the leakage site in FFA were recorded as RPE protrusion, RPE defect and RPE irregularity. HRS was defined as highly reflective dots present in inner and outer retina. Subretinal fibrinous exudates were defined as relatively hyperreflective clumps in subretinal space. Bridge was defined as sagging of posterior neurosensory retina.
Statistical Methods: Analysis was done using SPSS V16 software. For all tests, $P<0.05$ was considered to be significant.

Results

53 eyes of 50 consecutive patients were studied of which 45 were male (90%). The mean age of the patients was 40.14 ± 6.6 (Range: 25-57). The duration of symptoms ranged from 0 to 48 weeks with mean duration 7.13 ± 10.03 weeks. Only

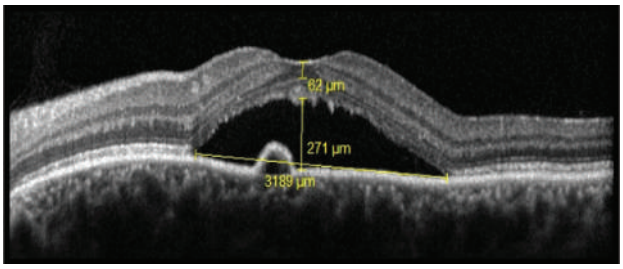


Figure 1- shows measurement of SRD width (3189μm), subfoveal height (271μm) of SRD and ONLT(62μm).

3 patients had bilateral central serous chorioretinopathy and the remaining were unilateral CSCR patients. The 13 eyes had recurrent disease (24.5%) and the others were initial cases 40(75.5%).

The average visual acuity among symptomatic eye was 0.17 ± 0.13 (0-0.60) and among fellow eyes was 0.004 ± 0.02(0-0.17).The average Sub foveal height, average maximum height and average width of SMD was 243.38 μm(0-960 μm), 284.1 μm (20-960 μm) and 3684.9 ± 1798.6 μm (739-7689 μm) respectively in symptomatic eyes. Among asymptomatic eyes, 2 had SMD with, mean maximum height of 4.68 ± 23.7 μm and mean width of 26.3 ± 179.9 μm. PED was present in 27 symptomatic eyes (50.9%) and 5 fellow asymptomatic eyes(10.6 %). Subfoveal SMD height and ONLT showed significant correlation with BCVA (P<0.05). ONLT was significantly decreased in symptomatic eyes (p=0.000, fig5). Commonest PED location was underlying SMD in all categories (fig3). Commonest type of PED was dome shaped in all categories except category C where low to flat PED was common. Among 27 leakage site, micro rip (figure 6), protrusion (figure 8) and irregular RPE (fig7) was seen in 12(44.4%), 13(48.1%) and 2(7.4%) sites respectively. Commonest leakage site morphology was RPE protrusion in category A, C, D and micro rip in category B (fig3). Hyperreflective dots (HRS, fig4) and bridge were seen in 43(81.1%) and 11(20.8%) symptomatic eyes respectively. Figure 2 shows comparison table between all four categories. Thickened outer photoreceptor layer (OPL) was more common in category A and thinned OPL was more common in category B (figure 2).

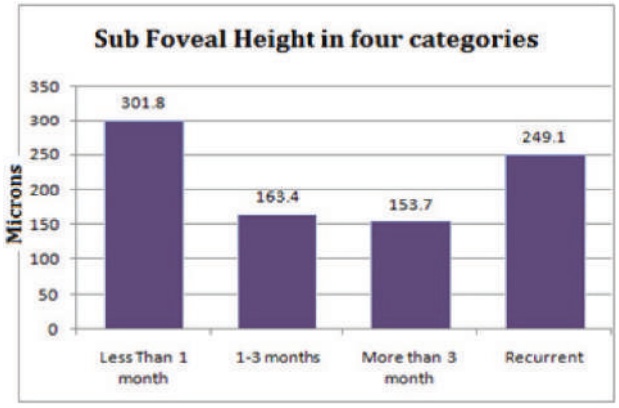


Figure 4 shows subfoveal height of SRD in all four categories.

		Less than 1 month	1-3 month	More than 3 month	Recurrent	P value
Number		23	11	6	13	
Age		38.04±4.9	41.09±4.44	46.17±8.18	42.23±9.18	0.04
Sex	Male Female	23(100%) 0	10(90.9%) 1(9.1%)	5(83.3%) 1(16.7%)	10(76.9%) 3(23.1%)	0.07
SMD	Sub Foveal Height	301.8(28-736)	163.4(33-46)	153.7(0-287)	249.1(26-960)	0.06
	Maximum Height	346.04(28-736)	214.9(20-594)	218.8(154-315)	263.15(26-960)	0.09
	Width	3678.5(1499-7291)	3922.6(1287-7689)	3426.5(739-7338)	3426.5(739-7338)	
PED Type	Dome shaped	9(81.8%)	4(80%)	1(33.3%)	7(87.5%)	
	Shallow PED	2(18.2%)	1(20%)	2(66.6%)	1(12.5%)	0.65
Outer photoreceptor layer	Thickened	17(73.9%)	1(9.09%)	3(50%)	8(61.50%)	0.00
	Thinned	2(8.69%)	10(90.9%)	3(50%)	5(38.5%)	0.00
	Disruption of OPL	4(17.39%)				

Fig 2 shows comparison between all four categories.

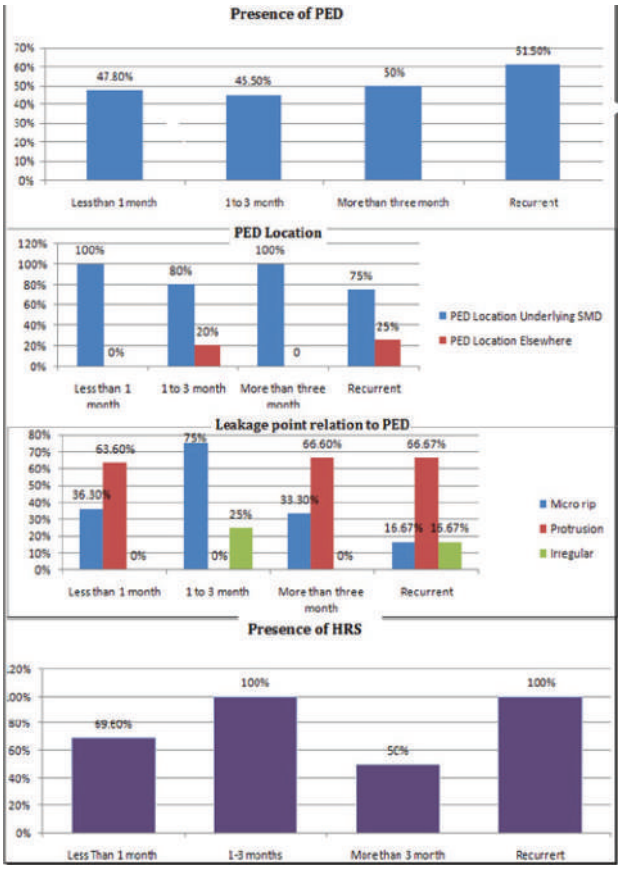


Figure 3 shows presence of PEDs, commonest location of PED, leakage point changes at RPE and PED as seen in OCT, presence of HRS in all four categories.

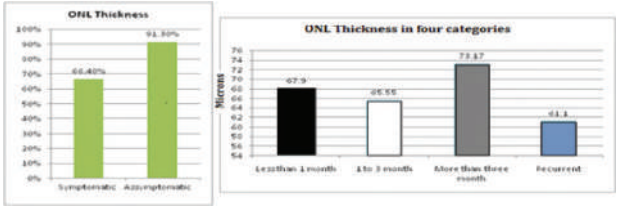


Figure 5 shows comparison of ONL thickness between as-symptomatic and symptomatic eyes and between all four categories.

Discussion:

In our study all patients were divided into four categories according to the chronicity of their symptoms based on subjective recall because there is no definite method for estimating the chronicity of CSCR to date.

We could demonstrate minimal SRD in 2 and PEDs in 5 asymptomatic fellow eyes respectively. Therefore often patients might not have any complaints even in the presence of SRD or PED if its very minimal. In a retrospective study of 76 eyes of 75 patients Seok et al has described relatively large sub retinal detachment (SRD) in early phase of acute CSCR.9 In contrast, the maximum height and width of SRD was comparable in all categories in our study though the sub foveal SRD height was maximum in patients with acute attack of CSCR presenting as initial or recurrent case (figure 4). The p value (0.06) was not very significant which could be attributed to small sample size. Similar to previous studies significant decrease in ONLT (figure 5) was seen in symptomatic eyes. Subfoveal SRD and ONLT showed significant correlation with BCVA ($P<0.05$). Masayuki et al has also described thinning of ONLT which begins in early phase and persist till the SRD persist. Faster resolution of SRD would prevent further cell death of photoreceptors. However significant visual loss occurs in cases with more than half a year period of SRD.[10] Similar to Seok et al study we have also demonstrated flat PEDs to be more common in chronic cases.[9] Bridge seen as sagging of posterior neurosensory layer could be granulation of posterior surface of detached neurosensory layer which could be observed in any stage of disease developed possibly due to shedding or disintegration of thickened outer photoreceptor layer that led to their eventual thinning. Seok song et al had described bridge to be more frequent in acute stages of disease and hyper reflective dots to be more common in chronic stages.[9] In contrast, in our study hyperreflective dots and bridge were seen in 43(81.1%) and 11(20.8%) symptomatic eyes respectively, and were comparable in all categories and thus not so reliable in determining the chronicity of disease. These hypereflective dots are thought to be composed of macrophages and remnants of disintegrated outer photoreceptors. Commonest leakage site morphology was RPE protrusion in all categories except category B where microrip was common. In all cases focal RPE proliferation was not present in conjunction with underlying RPE defects.[9] Soek et al has also described

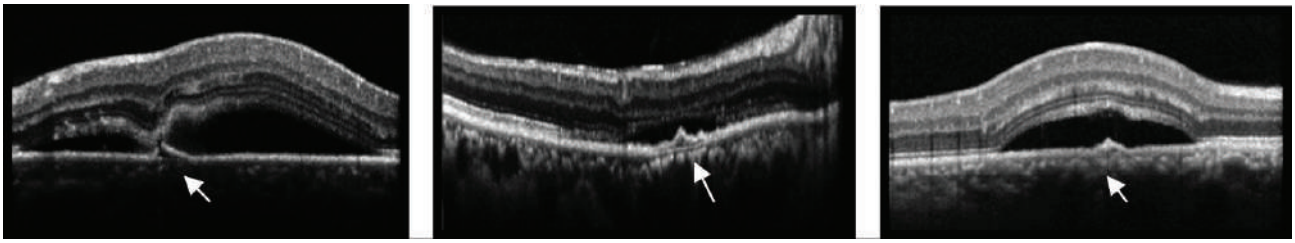


Fig 6: RPE defect at the leakage Fig 7: Irregular RPE at the leakage site Fig 8: RPE protrusion at the leakage site.

similar RPE protrusion frequently in chronic CSCR cases but in our study this was the most common RPE alteration at the leakage point.[9] In early phase of disease there was thickening of outer photoreceptor layer with thinning seen as the duration of disease increased. As the outer photoreceptor layer overlying RPE protrusion showed mild disruption, this protrusion could be result of reactive RPE change secondary to phagocytosis of outer photoreceptor fragments that has been shed earlier during the SRD.

The results of our study can be applied to various clinical scenarios. Firstly we can determine the chronicity of the disease based on the OCT findings and without completely depending on the subjective recall of the patient. Secondly we can select proper treatment plan based on SDOCT features. Shallow sub foveal SRD height, thinned out ONLT, thinned outer photoreceptor layer, shallow to flat PED are more suggestive of long standing disease with less possibility of spontaneous resolution and which can be treated with active intervention such as PDT or focal laser. We can expect spontaneous resolution of symptoms in patient with unclear time of subjective symptoms onset, but who showed bullous SRDs, dome shaped PED, thickened outer photoreceptor layer in their SDOCT images as these features are suggestive of acute disease. Third we can also give OCT guided thermal laser to areas of focal RPE defect, protrusion, focal irregular RPE with overlying areas of sagging of posterior neurosensory layer and mild outer photoreceptor disruptions suggestive of possible leakage site thus avoiding invasive procedures like FFA, especially in cases when they are contraindicated. Fourth it also helps to explain and prognosticate the disease to the patient.
Limitation of our study is small sample size in each group. The categories were formed on basis of subjective recall of patients so there may be some discrepancy regarding the exact duration of disease. Future studies with larger sample size and long term follow up would be necessary for better understanding of this disease.

Conclusion

Detailed morphological examination using SDOCT helps to understand pathological mechanism of CSCR and to identify the RPE abnormalities at leakage point which can aid in focal laser treatment in CSCR patients. Decrease in ONLT can help to prognosticate the visual acuity in CSCR patients. It also helps to determine the chronicity of disease and to plan the treatment options. Thus this simple, non invasive modality is an important diagnostic tool for understanding and treating CSCR.

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Surgical Technique

Simple New Technique for Scleral Fixation of IOL

Sinumol S MS,DNB, Mallika O U MS, DNB, Smitha Narayan MS, Sujatha N DO, DNB

Introduction

Scleral fixation of IOL is indicated in cases of aphakia with absent or inadequate capsular bag support. This includes aphakia following a large PC rent, following penetrating injury, in cases of subluxation or dislocation of lens, hypermature cataracts with weak zonules, pseudoexfoliation with zonular dialysis, microspherophakias etc.

An ideal method stabilizes the IOL in the ciliary sulcus without any tilt or decentration, and avoids damage to ocular tissue. This wonderful idea of scleral suturing of IOL was first described by Dr.Malbran et al in 1986.Later Dr.Lewis.J.S. popularised the ab-externo technique of scleral fixation in 1991[1]. Here 'rail-roading' of a straight scleral fixation needle with suture is done through a hypodermic needle ''inside'' the eye[2]. Numerous modifications came thereafter like knotless scleral fixation, sutureless scleral fixation, glued IOL[3] etc.

In sutureless scleral fixation[3,4] and glued IOL techniques[5], intraocular bimanual 'hand-shake' technique[6] is used.Here the haptics of the 3 piece IOL are grabbed through the respective sclerotomies using microvitreous forceps and exteriorised. Then haptics are tucked into scleral pockets dissected at the edge of the flap using 22G needle or 23G MVR blade.

Increased intraocular manipulations and surgical time will result in more complications.IOL tilt and decentration are problems, which result in poor visual outcome especially when the points of IOL fixation are not exactly at 180^0.

In this article, we shall explain a simple new method for scleral fixation of IOL. The key step is passing the scleral fixation needle and 10-0 prolene suture across the posterior chamber using a 26G 1.5 inch needle without any rail-roading or hand-shake "inside'' the eye.

Materials

1. 26G 1.5 inch disposable needle – 1no.
2. Double armed 10-0 prolene suture with straight needle at one end and curved needle at the other end- 2 nos.

Surgical Steps

Ensure a soft globe before surgery. After peribulbar anaesthaesia, conjunctiva is reflected from limbus at two sites 180^0 apart i.e., from 2'o clock to 3'o clock position and from 8'o clock to 9' o clock position in case of right eye and 3'o clock to 4'o clock position and 9'o clock to 10' o clock position in case of left eye. Adequate cautery ensures good haemostasis.

Partial thickness scleral tunnels with 2.5mm width are created in the above sites parallel to the limbus. For this first a 2.5mm horizontal partial thickness scleral incision is made close to the limbus and then tunneling is done with a crescent blade.Cutting the tunnels at the distal ends with vannas scissors create limbal based right angled triangular flaps diagonally opposite to each other(Fig 1).

Now the straight needle on 10-0 prolene is broken into half for easy manipulation and is docked into the lumen of the 26g 1.5inch needle "outside" the eye (Fig. 2).

This is passed through the temporal scleral bed 1mm posterior to surgical limbus, first perpendicular to scleral surface and once inside the eye, it is advanced across the posterior chamber parallel to iris plane to emerge at the nasal scleral bed1mm posterior to limbus exactly at 180^0 (Fig 3,7).A gentle pressure with fine forceps aids its exit(Fig7).

The straight needle with the10-0 prolene is retrieved. This delivery becomes easier as the length of the straight needle has been reduced to half of its original size before docking.

For additional strength, the double suture technique may be adopted, where another straight needle on 10-0 prolene is docked into the tip of 26g needle before it is withdrawn(Fig 4,Fig 8).
This suture is retrieved from temporal bed when the 26g needle is withdrawn from the eye (Fig 5, Fig 9).

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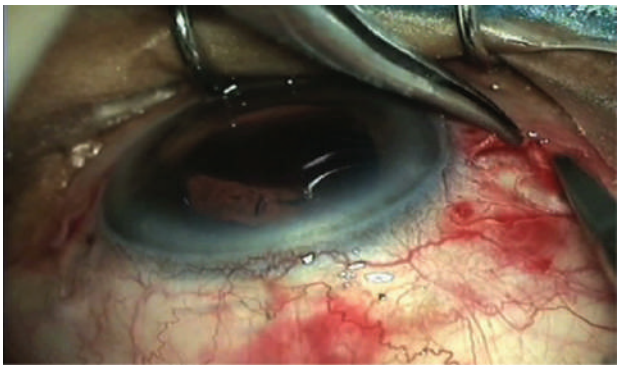


Fig. 1

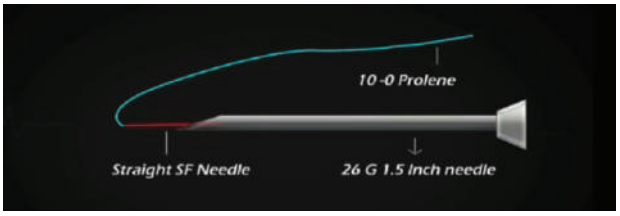


Fig. 2

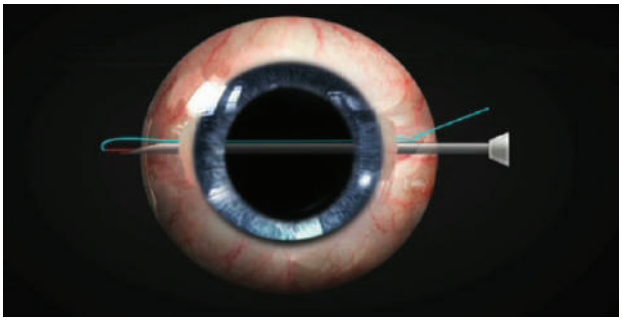


Fig. 3

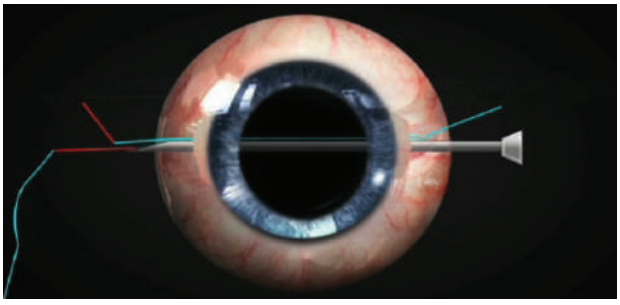


Fig. 4

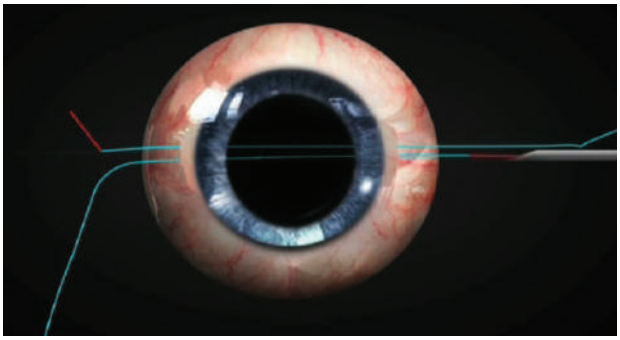


Fig. 5

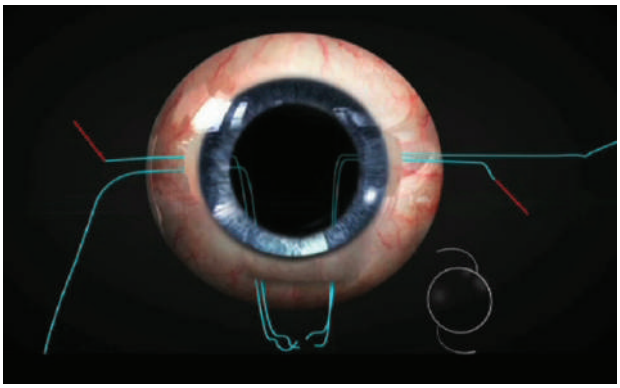


Fig. 6

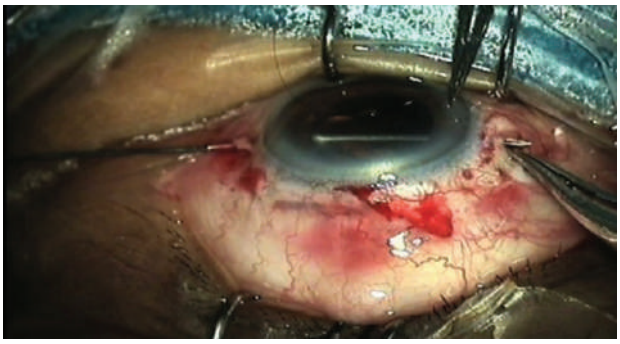


Fig. 7

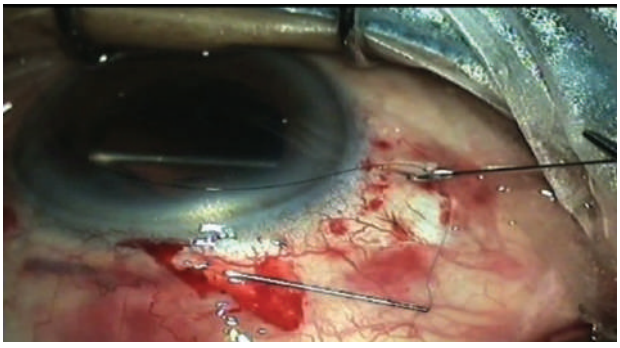


Fig. 8

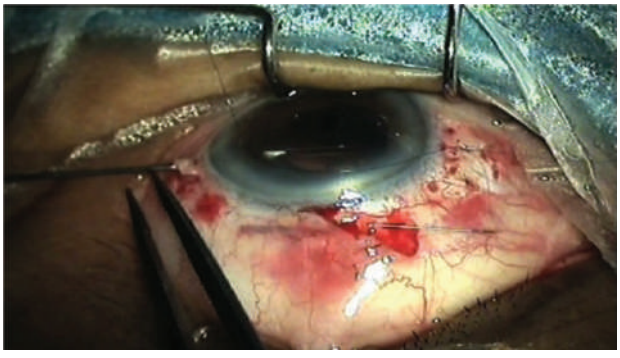


Fig. 9

Now two prolene sutures are traversing across the posterior chamber, with one curved needle and one straight needle at the ends on both sides under each flap.

Then a 6.5mm superior sclero corneal tunnel is made (optic diameter of rigid SF IOL is 6.5mm). Now the two sutures traversing the posterior chamber can be easily hooked out through the superior sclero corneal tunnel using a 26G needle bent at the tip or a Sinskey hook.The sutures are cut in the middle and are tied to the corresponding haptics of IOL. (Fig 6)

Each suture is knotted to the haptic eyelet once and then the suture ends are knotted together 7 times over. So the knot becomes easy as well as secure.

Now the IOL is introduced into AC and then placed in the ciliay sulcus and the prolene ends are made taut. Scleral fixation sutures are tied to each other after taking a small bite from the scleral bed with the curved needle on both sides(Fig 10).

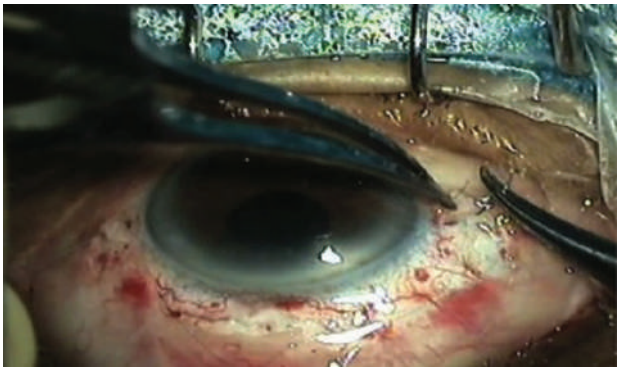


Fig 10

Scleral flaps are reposited and sutured with 10-0 nylon. Conjunctiva is repositioned(Fig 11).

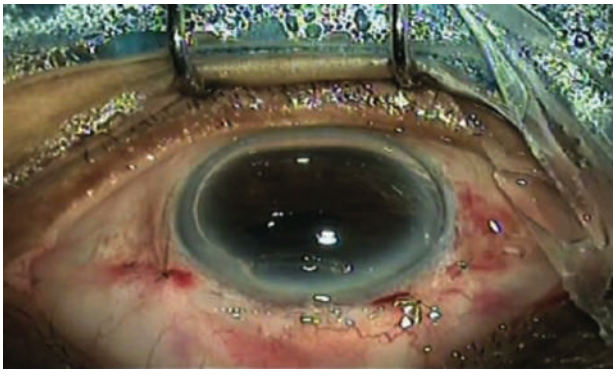


Fig 11

Advantages Of Our Technique

1. Sutures are passed exactly through 180^0. So there is no chance of lens tilt or decentration .
2. Single passage of needle across the posterior chamber is enough for the double suture fixation.
3. Minimum intraocular manipulation in this technique reduces chances of vitreous disturbances and traction, thereby reducing complications like retinal detachment, macular oedema and infection.
4. This surgery has a shorter learning curve and is less time consuming.

Caution

1. Removal of all lens matter is a must for this procedure.
2. A thorough anterior vitrectomy prevents vitreous incarceration.
3. Avoid scleral dissection and needle passage exactly through 3'o clock and 9'o clock positions to prevent injury to long ciliary vessels.
4. Keep the sutures 0.75- 1 mm posterior to surgical limbus. More posterior suturing will result in vitreous incarceration, greater inflammation and unstable fixation.

Management Of Subluxated IOL With This Technique

Subluxation or dislocation of IOL can occur post-operatively following blunt trauma. Spontaneous posterior subluxation happens after IOL implantation in PC rent. Surgery with IOL implantation in the bag for subluxated cataract even with a CTR also can go for subluxation and dislocation later.

In such cases where the IOL is visible in the pupillary area, we can adopt this technique for the IOL removal with simultaneous scleral fixation of IOL. For this, the 26G 1.5 inch needle is introduced with the docked straight needle

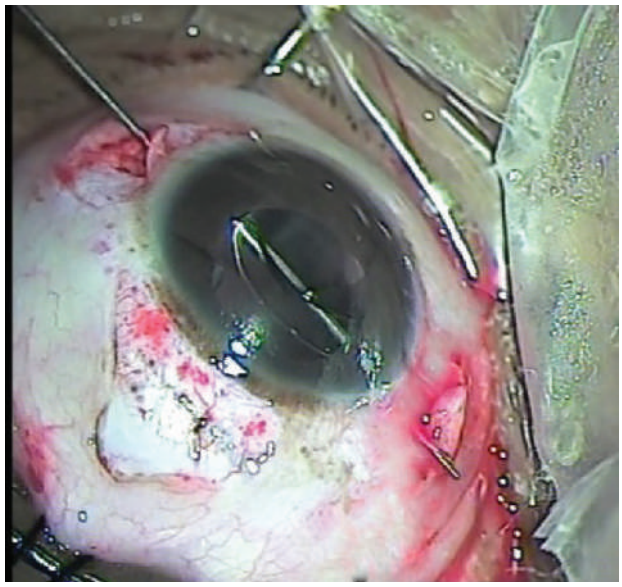


Fig 12

and 10-0 prolene through the temporal scleral bed and passed behind the subluxated IOL supporting it and then emerged out through the nasal bed as described earlier(Fig 12).

Now through a superior sclerocorneal tunnel, the subluxated IOL is removed. Adequate anterior vitrectomy is done. The straight needle with the10-0 prolene is retrieved from the 26G needle. Then another straight needle on 10-0 prolene is docked into the tip of 26g needle before it is withdrawn(Fig 4, Fig 8). Scleral fixation of IOL is done as described earlier.

To view this video, please visit: www.ksos.in

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Side Effects Associated with Prostaglandin Analogue Therapy

Dr.S.Deepthi DNB, Dr.S.J.Saikumar MS, DNB

The introduction of Prostaglandin analogues (PGA) in the mid 1990's was received with great enthusiasm because of its superior intraocular pressure (IOP) lowering efficacy and a near absence of systemic side effects. Almost two decades after its introduction however, a number of trivial and serious ocular effects are being reported.

Mechanism of Action

Immunohistochemical data have shown that the IOP reduction with topical PGF2-alpha is associated with a reduction of collagens within the uveoscleral outflow pathway. The ciliary body contains several prostaglandin receptors whose activation seems to stimulate a second messenger cascade for metalloproteinases synthesis which alter extracellular matrix modelling.[1]

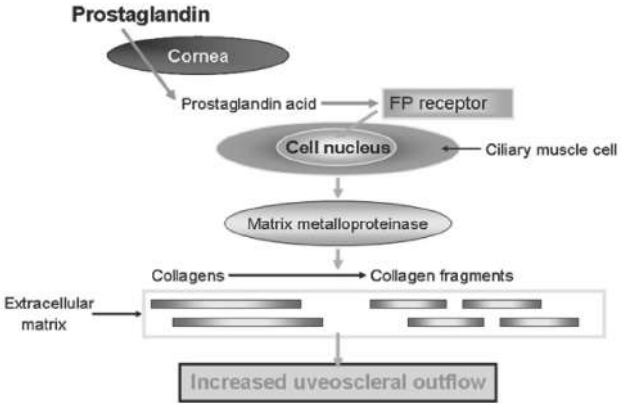


Fig 1. Mechanism of action of Prostaglandin analogues

Side Effects

Latanoprost being the first commercially available PGA has been the focus of most reported side effects. However available evidence suggests that currently available PGA's are comparable in terms of their side effects, except for a slight advantage of latanoprost with regard to conjunctival hyperaemia.

COMMON SIDE EFFECTS	LESS COMMON SIDE EFFECTS
Conjunctival Hyperaemia Eyelash changes Iris hyperpigmentation Periocular skin-pigmentation	Iris cysts Cystoid macular edema Anterior uveitis Reactivation of herpes simplex keratitis Prostaglandin induced periorbitopathy (PIP)

Common Side Effects

Conjunctival hyperaemia

Mild conjunctival hyperaemia is a common side effect of PGA's and is seen least frequently with latanoprost when compared to other PGA's. It usually occurs within the first 2 days of initiating treatment and declines over time.[2,3]

Conjunctival changes associated with prolonged use of Prostaglandin analogues

Chronic administration of topical PGA's has been shown to cause inflammation, scarring, keratinization and neovascularisation. Many studies show an increase in the number of fibroblasts and inflammatory cells in the conjunctival substantia propria and epithelial metaplasia. However, there is no conclusive evidence as to whether these changes are due to the prostaglandins or preservatives like BAK in these formulations.

Eyelash changes

Main changes in eyelash appearance include increased number, length, thickness, curvature and pigmentation. An increased pigmentation of the eyelid and periocular skin has also been reported. Eyelash lengthening is a fairly common side effect with between 45%-57% eyes affected after treatment for 6-12 months. Average increase in length of 0.7-0.8mm have been reported in various studies.[4]

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Fig 2: Hypertrichosis in a patient on bimatoprost in Left eye

Iris hyperpigmentation

It usually develops within first 8 months of initiating topical treatment.[5] Possible mechanisms suggested for iris pigmentation are stimulation of melanogenesis in iridial melanocytes, upregulation of transcription of the tyrosinase gene and migration of iris stromal melanocytes to thicken the anterior border region with no net gain in melanocyte numbers.[6] Uniformly brown irises appear to be at low risk for induced pigmentation. Uniformly blue/gray irises carry little or no risk for iris pigmentation, whereas heterogeneous hazel eyes especially golden brown or green brown are highly likely to develop iris pigmentation.[7] Iris pigmentation is a permanent change and does not disappear on stopping treatment.

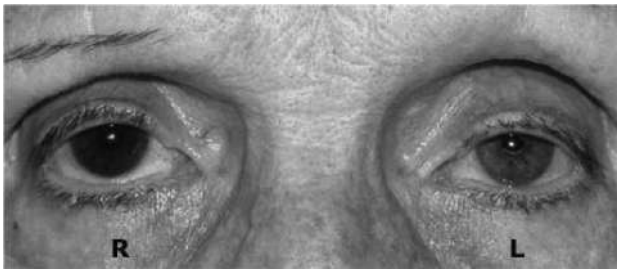


Fig 3: Iris hyperpigmentation in patient on bimatoprost. Iris hyperpigmentation is more evident in light coloured irides

Less Common Side Effects

Iris cysts

A rare event that may or may not have a direct association with PGA therapy is development of iris cysts. Cessation of medication was followed by decrease in size of the cyst with complete reversal over few months. Krohn and Hove have proposed that iris cyst formation might be related to flow pressures caused by increased uveoscleral drainage.[8]

Periocular skin pigmentation

Darkening of the skin of the lids or other sites around the eye is an occasional side effect. PGA induced pigmentation is most prominent in the eyelids and becomes apparent in few months though it can occur upto after 3 years. The prostanoid effects of melanogenesis and melanocyte proliferation have been suggested as possible mechanisms for skin pigmentation.[9] Skin pigmentation is reversible with normal coloration returning over a period of 7-8 weeks.[10]

Cystoid macular edema

Cystoid macular edema (CME) has been reported in few patients receiving topical PGA's but a causal relationsip has not yet been proved or disproved. In most cases CME appears weeks to months after initiating PGA therapy.[11] Furthermore the CME is reversible with early discontinuation of PGA and it has been shown that CME can be prevented with a NSAID. However, the risk increases if a PC rent occurs during cataract surgery.

Anterior uveitis

Prostaglandin induced uveitis seems to be due to a breakdown of blood-aqueous barrier and not really a inflammatory process (Arjomand et al). A comparative study of flare in patients on PGA's showed that after 3 months travoprost and bimatoprost had less flare than latanoprost which reflects a slightly superior break of the blood aqueous barrier by Latanoprost.[12] Uveitis usually resolves after discontinuation of PGA'S.

Reactivation of Herpes simplex keratitis

There have been a few case reports of reactivation of Herpes simplex keratitis(HSK) after initiating PGA therapy. Discontinuation of PGA is usually followed by resolution of keratitis in most of these cases.[13] Zimmerman et al analysed the data of 93,869 glaucoma patients for reactivation of HSK following administration of PGA's. The study revealed a rate similar to that found in the general population and did not correlate with any antiglaucoma therapy. It appears, therefore that the risk of activating an ocular herpes simplex infection through initiation of PGA is low.

Corneal toxicity

Dendritiform epitheliopathy has been reported after latanoprost treatment. Few studies have shown episodes of mild punctuate epithelial erosions.

Prostaglandin Associated Periorbitopathy

Deepening of upper eyelid sulcus
Upper eyelid ptosis
Involution of Dermatochalasis
Periorbital fat atrophy
Mild enophthalmos
Inferior scleral show
Increased prominence of lid vessels
Tight eyelids



Fig 4: Patient instilling bimatoprost in left eye. Left eye shows deepening of inferior and superior sulcus due to fat resorption, with inferior scleral show and periorbital skin depigmentation

In a study, periorbital fat loss was the most frequent finding and was observed in nearly all PAP patients. Frequency of PAP was most with bimatoprost group and least with latanoprost group. The frequency of milder changes (the presence of either only periorbital fat loss or dermatochalasis involution or the presence of both) was higher in the latanoprost group than with travoprost and bimatoprost.[14]

Systemic Side Effects

Occasional systemic side effects have been reported. These include gastrointestinal disturbances similar to those caused by aspirin or other nonsteroidal anti-inflammatory agents, chest pain, palpitations and upper respiratory tract infections.

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Diagnostic Challenge- Refractive Surgical Problem

Dr V Sujith Nayanar MD, DNB, FRCS

A 21 year old female was referred to me on the first postoperative day following refractive surgery with drop in vision in the left eye. The pre-operative records from the referring doctor were reviewed in detail. As per the records the patient presented herself for correction of refractive error for cosmetic reasons. Her refractive error was:

	OD	OS
UCVA	6/36	6/24
Refraction	-1.5/-0.5 x 1500	-1.0/-1.0 x1200
BCVA	6/6	6/6

Anterior segment evaluation under slit lamp examination was within normal limits. Fundus evaluation was also within normal limits. Old records revealed single recording of high IOP (OD=26mmHg and OS =28mmHg) during one of her visits couple of years back. Gonioscopy performed at that time was normal with open angles. No family history of glaucoma or Ocular hypertension is recorded. Her elder sister underwent LASIK couple of years back with satisfactory visual recovery. Routine pre LASIK work up were performed. Orbscan (fig 1) report revealed normal study except bilaterally symmetrical steeper km with good pachymetry and satisfactory posterior elevation data.

She underwent uneventful LASIK surgery on 03.12.13 using Technolas* 217P (100Hz) machine and Zyoptix X P micro keratome. A 120 micron flap was cut with single blade (fresh use) for both eyes and right eye was performed first.

Post-operative treatment was:

- E/d Zymaxid QID*
- E/d Lotepred QID*
- E/d Systane Ultra QID /SOS*

On the first post-operative day (POD), she had complete visual recovery of 6/6 in right eye. But left eye was recorded

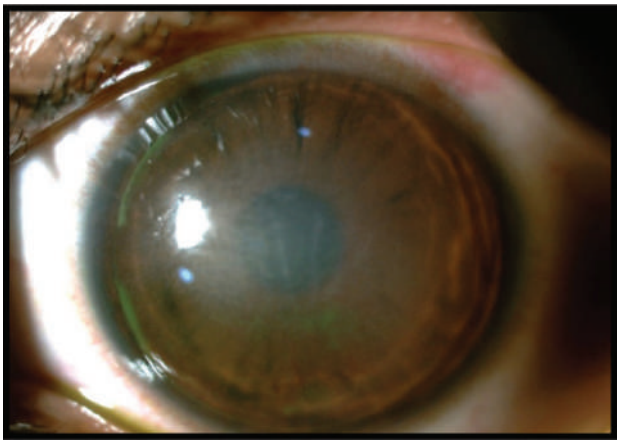


Fig 2: Clinical picture on POD 1

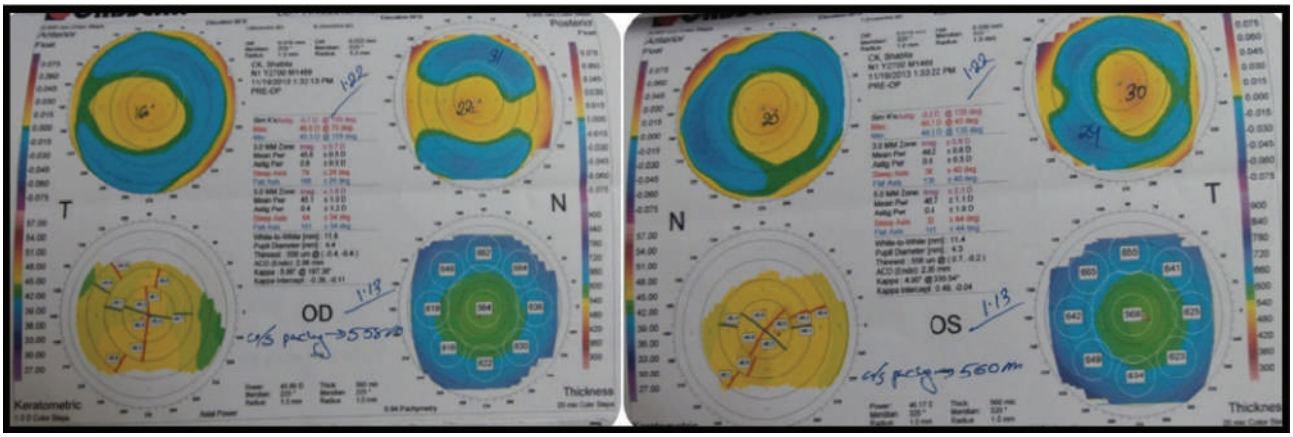


Fig 1: Pre op Orbscan

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as having CFCF (counting fingers close to face) and the patient was referred to us. On examination, the left eye showed dense central corneal edema. (Fig 2). On closer examination, it was noted that the edema was predominantly

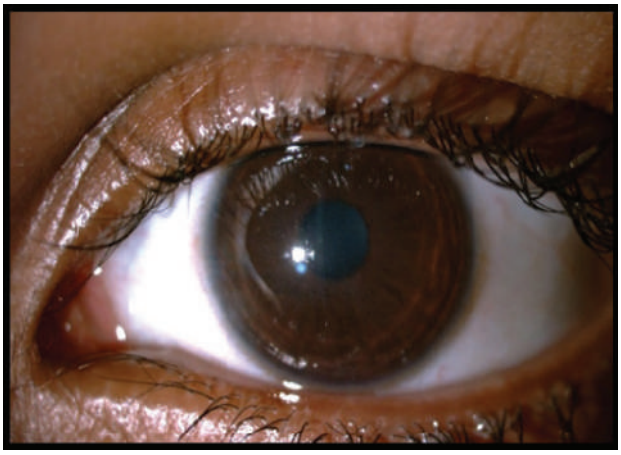


Fig 3

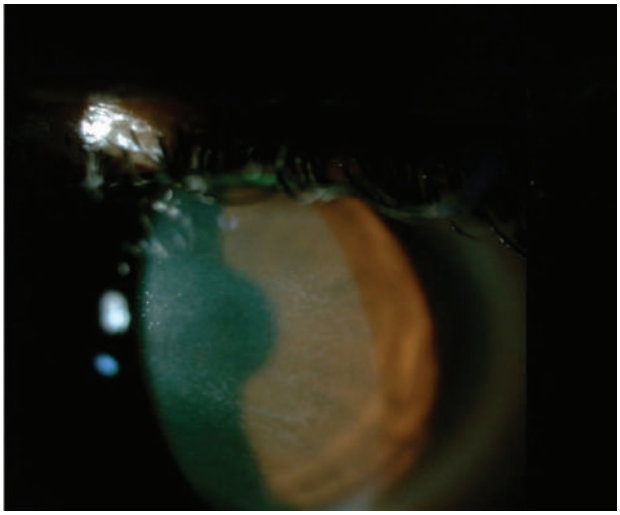


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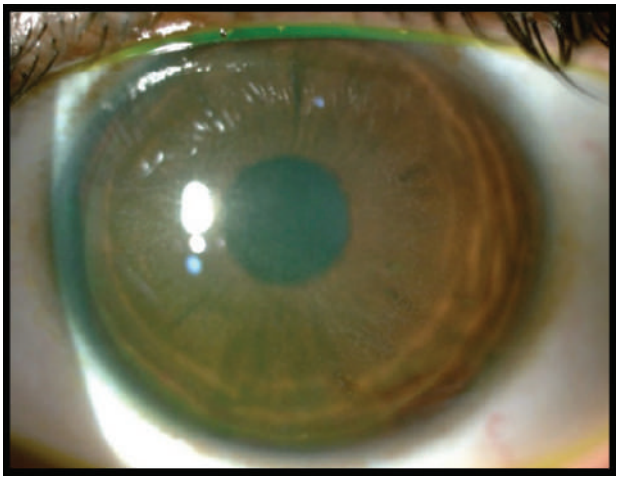


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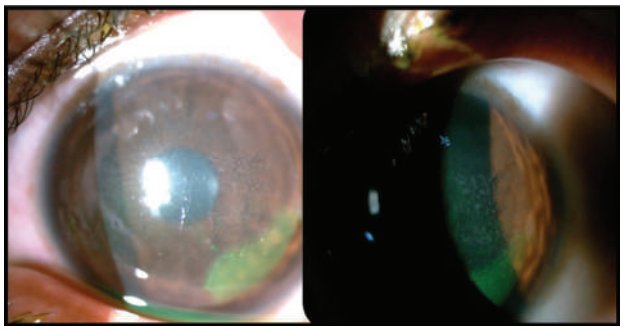


Fig 6: Progressing epithelial ingrowth and epithelial defect at 3-5 o'clock hour zone

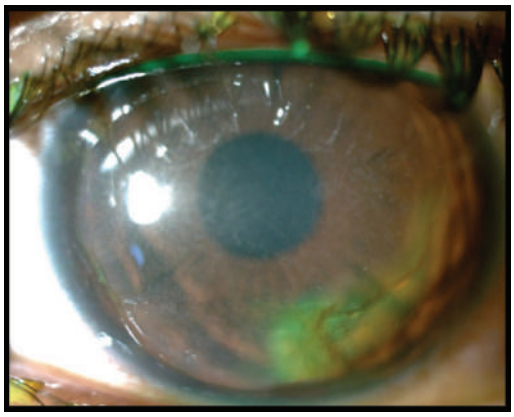


Fig 7: Flap melt at the infero temporal zone

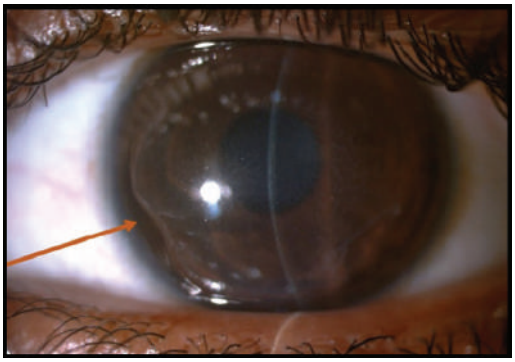


Fig 8: Progressing new lesion of flap melt

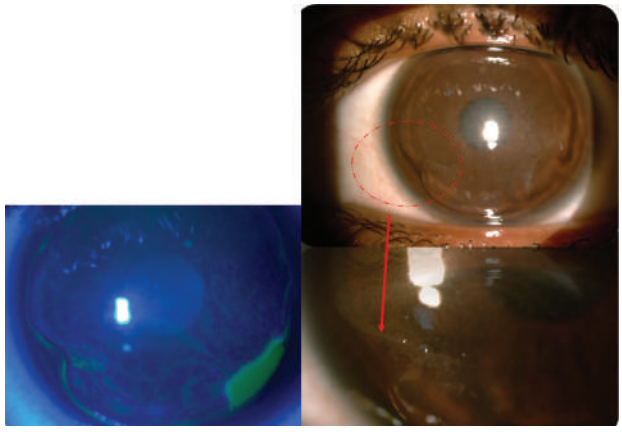


Fig 9: Progressing flap melt both sides

involving stromal bed with only minimal edema of the flap and no interface fluid. The IOP was 18mmHg on non-contact tonometry. Central DM folds were also evident.

Though not convincing, a provisional diagnosis of DLK (Diffuse lamellar keratitis) Stage III was made and topical steroids were increased along with hypertonic saline drops. Patient was reviewed daily for 3-4 days. No change in clinical picture was noted. In view of her previous recordings of high IOP and well known fallacies in IOP measurements after LASIK surgery and in edematous cornea, trial of oral acetazolamide (DIAMOX) was given. IOP recording after 2 days revealed 11mmHg with no improvement in edema.

Next clinical differential diagnosis was PISK (pressure induced stromal keratitis) due to interface fluid which is attributed to steroid response. Though clinical picture in slit lamp examination did not reveal interface fluid, the steroids was stopped abruptly to see the response. After 3 days (POD 10) the edema was found to be resolving and subjective improvement in vision was noticed. IOP was 14mmHg. By POD 14, edema was well resolved and IOP was 12mmHg (fig 3). As edema resolved, evident signs of DLK were visible though the vision recorded was 6/12. Hence prednisolone was cautiously restarted under cover of hypotensive agents. One week later (POD20) the vision improved to 6/9 with signs of resolving DLK and IOP of 17mmHg. Early signs of epithelial in growth as peripheral pearls were noted in this review visit (Fig 4,5). The steroids were tapered and patient reviewed after 10 days (POD 1month) to evaluate the progression of epithelial ingrowth.
Fig 3,4, 5 : Edema resolved. Interface haze due to DLK and epithelial pearls of ingrowth

The epithelial ingrowth was found to be progressing fast with islands of epithelial pearls reaching pupillary zone. An epithelial defect was noted localized to the infero-temporal region for about 2 clock hours. BCL was applied. Vision was 6/18 with pinhole improvement to 6/9. On subsequent days the flap tissue loss at the site of epithelial defect was noted, which hinted towards progressive flap melt (fig 6,7). To control inflammation stronger topical steroids was started (Difluprednate tid). Two days later fresh zone of tissue loss was noted medially (POD6weeks) (fig 8).

Third differential of a viral etiology was also considered and short trial of oral Acivir was also given. IOP again increased to 28mmHg. Hence Difluprednate was withdrawnas no clinical resolution of inflammatory signs was noted. In the subsequent days IOP was managed with hypotensive agents but relentless progression of epithelial ingrowth and flap melt was noticed from both sites (fig 9).

Perplexing questions in this situation are:

1. What caused unilateral edema?
2. How reliably could have IOP been recorded in such cases?
3. How to manage inflammation and DLK in steroid responsive patient?
4. Role of systemic steroids in such situations?
5. Intervention to be planned – what and when ?
6. Effect on final visual outcome?

In the subsequent discussion we will try to critically evaluate this case as what was the cause for this anomalous behavior of 'one eye'. Valuable inputs from the experts in the field of cornea and refractive surgery are discussed as how they would have managed this case and how this case has to be managed further to tackle the present scenario.

Discussion:

1) Dr Anil Radhakrishnan

This case though indeed interesting and thought provoking is extremely difficult to handle as a practitioner. With the benefit of hindsight, I would venture to make a few observations regarding this.

1] Though, routine IOP measurement [with applanation tonometry or non-contact tonometry] is inaccurate after LASIK, unilaterality of the condition and onset within a day almost rules out interface fluid syndrome or pseudo-DLK [Diffuse Lamellar Keratitis like picture due to IOP elevation]. Also, steroid induced IOP elevation usually takes a few weeks, at least a week to manifest [4].

2] The fact that there was intense inflammation right on the first postoperative day, involving the posterior stroma do suggest that there was a source of inflammation implanted in the left eye during the procedure.

3] On day 2, there were cellular aggregates in the interface with central corneal edema, with relative clearing in the periphery [as compared to day 1, very suggestive of stage3 DLK. Lifting of the flap and cleaning of interface is recommended at this stage to prevent permanent sequelae like scarring or flap melt, which can happen in a significant proportion [1,2] .

Personally, I would have preferred to start systemic steroids on day2 and gone ahead with surgical treatment [flap lifting & cleaning] had there been no improvement within a day.

4] On day 14, even though there is decrease in corneal edema, there are cellular aggregates in the interface with early flap melt between 4 to 5'o clock. The use of Matrix MetalloProtienase [MMP] inhibitors – preferably medroxyprogesteroneeyedrops, systemic steroids and

doxycycline is likely be useful at this stage [1,3,5,8].

MMPs are a family of extracellular endoproteinases that can degrade all components of extracellular matrix and basement membrane. They are synthesized and secreted by a variety of cells including corneal epithelial cells, fibroblasts and inflammatory cells. MMPs are secreted as pro-MMPs requiring extracellular activation and their activity is regulated by specific tissue inhibitors of MMPs [TIMPs]. The balance between the two is important in maintaining tissue architecture [1,6,7].

Flap melt is usually a culminative event of inflammation 1,3,7,8. Following an acute stimulus, pro-inflammatory cytokines mainly IL-1ß and TNF- alpha are released, which brings in more PMN &Langerhan's cells , upregulates the inflammatory cascade, activates complement and increase expression of all three major categories of MMPs [gelatinases, collagenases &stromelysins], which results in tissue breakdown.

Flap melt is mostly unilateral and occurs 2-5 weeks after LASIK. In most cases there is an intraoperative or early postoperative complication viz, epithelial defect involving flap edges, irregular flap, excess manipulation of flap, re-lifting of flap for enhancement, DLK or epithelial ingrowth. About 40 – 50% of cases are associated with systemic diseases like rheumatoid arthritis, SLE, thyroiditis, Sjogren's syndrome in which LASIK may be an inducing factor 1,5. It is described as a self-limiting condition, which leaves varying degrees of corneal opacification[1].

As mentioned before, it is much easier to make decisions in hindsight, looking at the progress of events by commenting on clinical pictures kept in a chronological order. The task of encountering such a rare unfortunate patient and making decisions facing a lot of unwelcome questions is indeed an onerous one.

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2) Dr Anand Parthasarthy

On going through the Case records it was a difficult case to manage with relatively rapid changing clinical picture on each visit. It is commendable that the treating doctors have documented it.

My comments are as follows

1. Choice of the Procedure- With a refractive error of -1.5 D , I would have definitely preferred Surface Ablation as my top choice rather than a LASIK since visual results are same , in addition the Flap does induce additional aberrations which affect the quality of vision in these patients
2. A Previous suggested History of raised IOP, I would have been cautious with steroid use. Regarding the Intra Operative steps, it is not mentioned whether, the same microkeratome blade was used in both eyes, whether there were any other patients operated on that day were the outcomes any different in them. Marking Microkeratome flap edge is a preferred intraoperative step
3. If we see the picture on Day 1 carefully, slight flap misalignment is noted on the nasal side, intraoperative marking could have prevented this. The asymmetric presentation is definitely unusual; my initial diagnosis on seeing the patient during the first week would have been Steroid Response knowing that GAT and Non Contact Tonometers give false lower readings.

Edema resolves following stoppage of the steroids giving the diagnosis of steroid response more credence

4. Week 2 pictures suggest multiple areas of epithelial ingrowth (Not DLK!!) which then enlarge to become large epithelial nests affecting vision. An early intervention with an

interface wash and epithelial cell sheet removal is warranted urgently at this stage, a preoperative identification of areas of ingrowth at the slit lamp and marking them to make sure all areas are identified intraoperatively. Using described chemical agents or manual removal can be done, meticulous removal of the epithelial nests on the flap bed and underside of the flap is imperative. Sutures or Fibrin Glue to the edge where there is ingrowth would help good flap adherence and prevent recurrence.

5. One month post op, it is becoming more difficult to manage but a very gentle flap lift and following the steps described in point 4 is still possible and would salvage the situation even at this advanced stage of epithelial ingrowth. Use of fibrin glue at the flap edge along would be help to bridge the areas of stromal loss.

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Chennai

3) Dr J K Reddy

This is one of the most complicated cases I ever saw in my refractive surgery practice. The picture on 4 th December(POD1) is very definitive of DLK. It should respond to topical/ systemic steroids. In fact a close look at day 1 and day 7 photographs shows an improvement with decreased stromal edema. What is so special about this case is the epithelial ingrowth complicating the early late post-operative period. The flap melting is well known phenomenon with epithelial ingrowth, but the flap necrosis is also reported with acute severe DLK. It is a bit difficult to take a decision of epithelial scrapping in view of the thin and partially melted flap

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Sankara Eye Hospital, Coimbatore

4) Dr Srinivas K Rao

A flap of 120 microns was planned. The second eye often has a thinner flap if the same microkeratome blade was used. Since intraoperative measurements are not available and there is no postoperative OCT data, this premise cannot be confirmed. The color clinical photo on POD 1 shows some fluorescein pooling / staining at the nasal periphery of the flap. Although the severe localized central edema suggests central toxic keratitis, the subsequent behavior and diffuse DLK suggest otherwise. In the context of edema, and the initial fluorescein pattern, it is possible that there was some flap shift / retraction (due to a possible combination of thin flap and edema). These could have predisposed to the subsequent significant epithelial ingrowth. The subsequent pictures at 1 month indicate the presence of staining and melting limited to the flap. This feature and the lack of a dendritic appearance make the likelihood of a viral pathology unlikely. At 1 month, although the changes are in the inferotemporal region of the flap, edema of the nasal edge is also noted. This is the area that subsequently melted! ! Poor healing of the stromal interface can be seen with DLK and this can predispose to epithelial ingrowth, especially if there is also poor apposition of the flap edges with the underlying bed. The subsequent melting could be due to the epithelial ingrowth. ! ! The DLK management would include the use of topical steroids, as done here. In retrospect, given the severity of the DLK and the early epithelial ingrowth, perhaps the use of oral steroids for the DLK (to allow better healing), and early flap lift and wash of the interface may have helped. Once the flap melt occurred secondary to the epithelial ingrowth, early surgery to fix the problem, might have helped avoid the nasal melt. Adjuncts like oral doxycycline and Vitamin C can be used (and were probably tried by the treating physician)! ! At this time, treatment of the epithelial ingrowth by flap lift, scrape and suturing of the flap edges to promote healing may be recommended - although the significant distortion of the flap from the melt may interfere with the visual outcomes. If this fails, excision of the flap may be necessary! !

Dr Srinivas K Rao
Darshan Eye Clinic
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5) Dr Rajesh Fogla

This 21 year old female who underwent uncomplicated LASIK procedure in both eyes, had an unusual complication in her left eye. From the sequence of events it seems possible that multiple factors could have been responsible for the clinical situation. The initial clinical picture immediately post LASIK appeared similar to a grade 3 or 4 diffuse lamellar keratitis (DLK) or pressure induced stromal keratitis (PISK) Although the IOP seemingly appeared normal it is to be noted that applanation tonometry gives false low IOP values due to presence of fluid in the interface (anterior segment OCT would have helped in this situation to diagnose the condition more effectively). From the clinical pictures it appears that on day 2, there was some amount of fluorescein staining at the flap edge (which is unusual, and can be explained by the retraction of flap edge due to flap oedema). Discontinuation of steroid therapy on day 7 appeared to improve vision again indicating that raised IOP (steroid responder) could have been responsible for the sequence of events post LASIK. Due to all these events, it is possible that the flap edge did not appose properly in the postoperative period, leading to

peripheral epithelial ingrowth. Persistent inflammation and release of proteases from the epithelial cells in the interface could be responsible for the flap melt, although a thorough systemic evaluation needs to be performed to rule out collagen vascular disease such as rheumatoid arthritis.

How I would have managed this difficult case - well almost quite similarly, though I would have kept PISK higher on my list of possible aetiology, monitored IOP using tonopen on the peripheral corneal beyond the flap edge. Switching over to weaker steroids such as loteprednol or fluorometholone, which have a lower tendency to raise intraocular pressure, oral acetazolamide to control IOP and topical hyperosmotics to assist resolution of flap oedema are the medical options at this stage. Oedematous flap adhesion is not very secure; hence a bandage contact lens could have helped ensure flap stability. Once the peripheral epithelial ingrowth is noted with epithelial melt, flap lift clear the ingrowth should have been considered, followed by bandage contact lens placement. Collagen cross linking could be considered to limit the flap melt as well.

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To summarise

To plan further treatment first of all we have to first analyze the situation and understand what was the etiology and course of events that led to this scenario. After the case was submitted to discussants an anterior segment OCT was performed which revealed a thin flap (~60 micron) in the left eye, whereas right eye flap was ~120 microns. Also the patient was ruled out of any collagen vascular disease which was done after the case report was sent to the participants for discussion.

The presentation with central corneal edema may be associated with following conditions:

1. Central Toxic Keratopathy (CTK)
2. Diffuse Lamellar Keratitis (DLK)
3. Pressure Induced Stromal Keratitis(PISK)

But presentation on day 1 rules out PISK. Between CTK and DLK, the predominant involvement of stroma posterior to interface supports CTK. The Central Toxic Keratopathy (CTK) syndrome describes a rare, acute, non-inflammatory process that results in dense opacification of the central corneal stroma after refractive surgery1. Although striae are a characteristic feature of CTK, the condition can exist in the absence of striae. The findings in CTK typically resolve between 2-18 months

Since the centralized stromal haze in CTK spontaneously resolves within 18 months without treatment, close monitoring and regularly-scheduled follow-up remains the primary management strategy in patients with CTK. Although corticosteroids were used in the past, the recent discovery that CTK is non-inflammatory in nature coupled with the fact that CTK is unresponsive to steroid therapy have discouraged the use of these medications in the management of CTK. Furthermore, and perhaps more importantly, CTK is oftentimes preceded by DLK 2 particularly during postoperative days 1 and 2.

More importantly, many eyes with DLK grade 4 typically develop classic clinical manifestations of DLK grade 1-2 over the first two weeks with the characteristic peripheral lesion gradually transforming into central grade 3 and grade 4 over the course of 3-5 weeks. DLK Grade 4 rarely occurs within the first 3 post-operative weeks whereas CTK yields classic findings within the first 3-7 days after surgery.

So we are forced to assume that some intra operative irritant factor predisposed the 'second eye' to a severe CTK on day 1 with an underlying component of co existent DLK. The role of steroid responsive IOP rise is debatable due to its presentation on day 1 . It seems to have some effect in worsening the situation, which is not fitting into the pathogenesis as per our present understanding of the condition. But non responsiveness to steroids support CTK and abrupt stoppage of steroids could have worsened DLK which surfaced out as CTK resolved spontaneously.

Another debatable issue was regarding the lifting of flap and interface wash and the timing for the same. Although lifting the flap and irrigating the interface can provide benefit

in reducing inflammation in early stages of DLK, given the non-inflammatory nature of CTK, irrigation of the interface does not confer benefits in CTK haze. In fact, irrigating beneath the flap in CTK can be deleterious in so far as it may exacerbate existing tissue necrosis, precipitate a buttonhole of the flap, increase the chance for epithelial ingrowths, and lead to keratocycte apoptosis in the stromal bed. Furthermore, irrigation of the flap can increase thinning of the residual stromal bed leading to an early increase in hyperopia due to augmented anterior corneal flattening. The undesirable outcomes associated with raising a post-surgical flap (i.e., development of a buttonhole from tissue loss and the potential for decreased BCVA), should be given prior consideration in patients in whom the diagnosis is uncertain.

Regarding the accuracy of IOP readings post LASIK, Dr Fogla's comment is very well taken and the surgeons are advised not to take pressure readings on the center of the flap, but on the periphery where the true pressure will be found. You maybe get a 10 to 20 mm Hg reading in the middle if you are sensing the IOP in the fluid pocket, but the pressure measured peripherally might be as high as 38 or 40 mm Hg.

As many of our discussants have rightly noticed the flap edema and thin flap cause poor adhesion of flap at the margins and to the bed which predisposed to epithelial ingrowth in to the potential space below the flap. Early signs of epithelial ingrowth were probably missed out due to edema and interface haze. Inadequate steroids use led to flare up of DLK which might have co existed with edema. Late management of epithelial in growth led to flap melt which is result of the inflammation. The pathogenesis of melt is well discussed by Dr Anil. Late management of DLK led to persistent haze.

Role of anterior segment OCT was mentioned by our experts which is very valid in this case. The non availability of the investigation at the right time deprived us of valuable evidence of ruling out fluid in the interface in the initial days. The flap thickness was later confirmed which helped in hypothesizing few points.

On retrospective evaluation, role of systemic steroid was also underestimated in this case as pointed out by our experts especially in the scenario of suspected steroid responsiveness.

How case was managed further

At the point where progressive flap melt was noticed from both sides with confluent areas of epithelial ingrowth involving the pupillary zone the patient was taken up for flap re lift and interface scraping off of epithelial pearls and wash. A bandage contact lens was maintained for 10 days. The response was good with no recurrence of epithelial ingrowth for up to 1 month post op. Role of fibrin glue at this stage for better adhesion of flap edge after re lift , as mentioned by Dr Anand, is well accepted. At 2 months post operative period the vision in the left eye is 6/12p (0.25/-0.50 x800) with persistent interface haze and IOP maintained normal.

Potential steps in future

If the patient is unable to adapt with present vision, possible procedure for better unaided vision includes femto-second laser assisted superficial lamellar keratoplasty without sutures. The role of anterior segment OCT in planning this procedure needs to be underlined.

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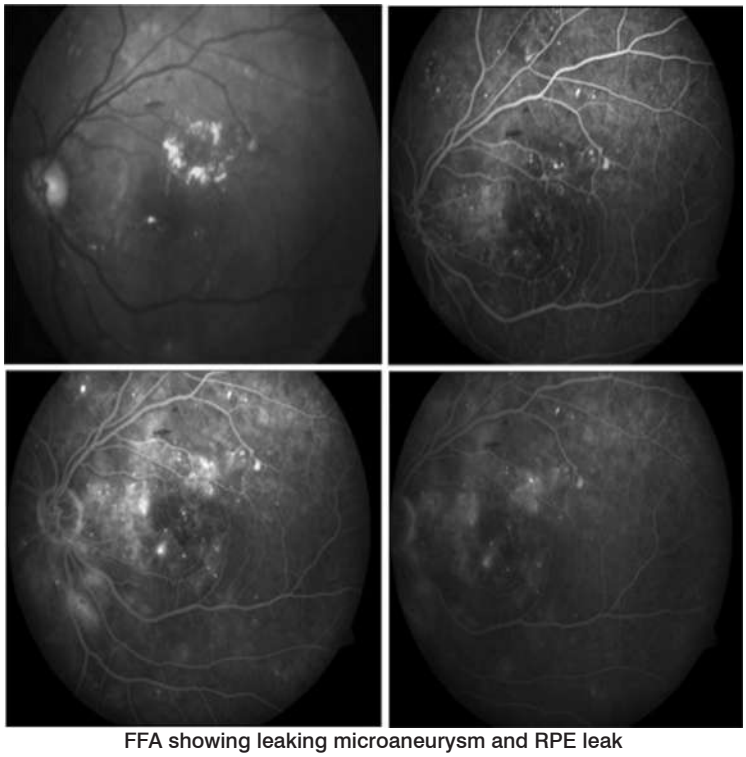
Acknowledgement

Dr J K Reddy for co-managing this patient.
Dr Anil Radhakrishnan, Dr Rajesh Fogla, Dr Srinivas K Rao, and Dr Anand parthasarthy for participating and contributing to this session.

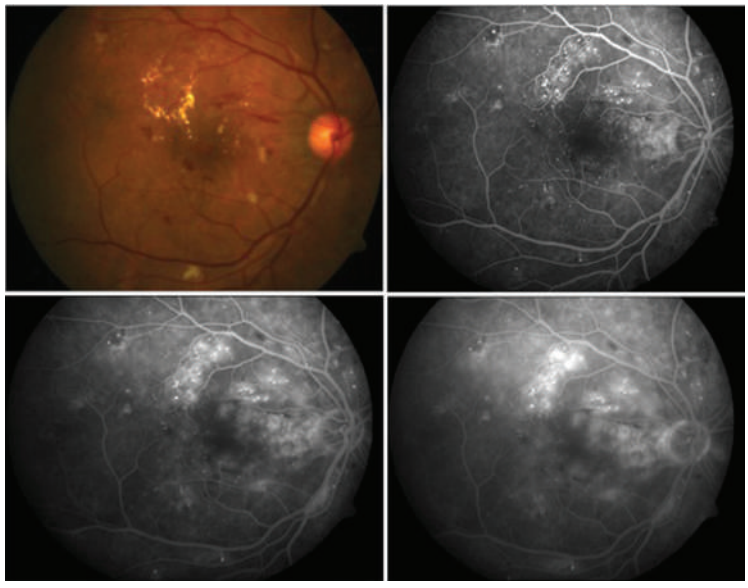
* Financial interests declare: none

Mahesh Gopalakrishnan MS, DO, DNB, FRCSEd.

46 year old diabetic patient with Severe NPDR and CSME both eyes. FFA shows leaking Microaneurysms in both macula. OCT shows large serous macular detachment with spongiform oedema. Fundus autofluorescence shows hyperautofluorescent area in both eyes suggestive of underlying central serous Chorioretinopathy (CSCR). FFA of left eye shows the leak increasing in late phase which would have been diagnosed as leaking microaneurysm. Fundus autofluorescence picture gives the clue for diagnosing CSME with underlying CSCR

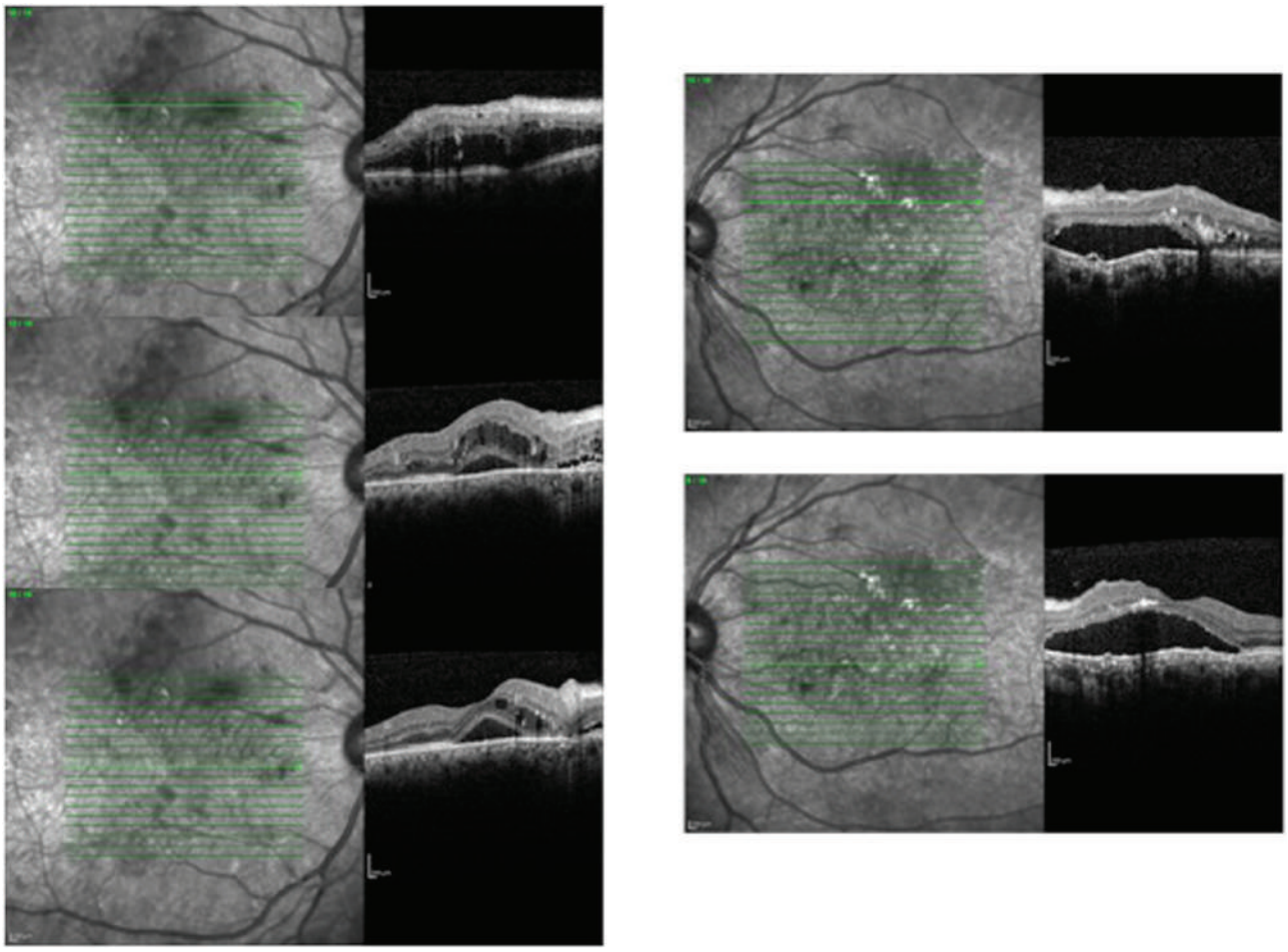


FFA showing leaking microaneurysm and RPE leak

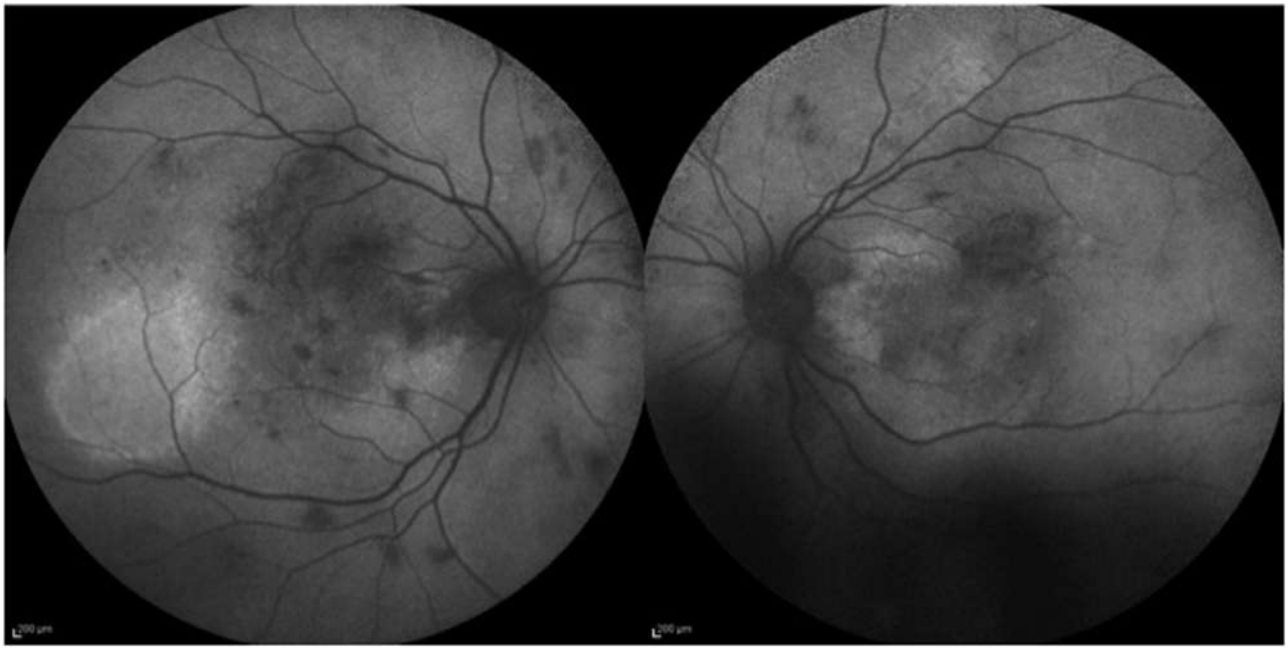


FFA showing leaking microaneurysms

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OCT showing out of proportion serous detachment



Fundus Autofluorescence diagnosing CSCR

Brief Report

Purtscher's Retinopathy

Rekha.S MBBS, Rajesh.P MD, Moinul Haq MD, DM

Case 1

A young male presented with loss of vision in left eye following a road traffic accident .There was history of a heavy object falling on the chest at the time of the accident. He did not sustain injury to other organs or bones, but was unconscious for few hours and was kept under observation in the hospital for few days

Vision at presentation was 6/6 in right eye and CFCF in left eye. Anterior segment examination was unremarkable.

Left eye fundus showed patches of opaque retina in the posterior pole with relative clearing around the vessels. There were few areas of preretinal hemorrhage also (Fig-1). Right eye fundus was normal (Fig -2)



Fig - 1



Fig - 2

Case 2

A female presented with decreased vision in both the eyes eighteen days after a normal vaginal delivery. The vision started deteriorating two days postpartum and gradually worsened to become CFCF both eyes . There was history of Pregnancy induced hypertension and post partum psychosis . Fundus examination showed patches of pale retina with pre-retinal hemorrhage in left eye and opaque retina in posterior pole resembling CRAO in right eye (Fig-3 &4). Detailed cardiovascular evaluation and coagulation profile were normal

Discussion

The clinical presentations in these patients describe a rare ischemic retinopathy called Purtscher's retnopathy. The first patient was initially diagnosed as combined CRAO and CRVO and the second patient was referred to us with a diagnosis of CRAO.

Both the patients received treatment with high dose IV methylprednisolone, with no benefit.

Purtscher's retinopathy

Purtscher's retinopathy was named after an Austrain ophthalmologist, Othmar Purtscher.[1,2] He described this in 1912 , as a cause of sudden vision loss in patients with head trauma, characterized by multiple white retinal patches and retinal hemorrhages.

Since this first report, similar retinal appearance has been observed in many nontraumatic conditions also. The associations of Purtscher's retinopathy reported are:

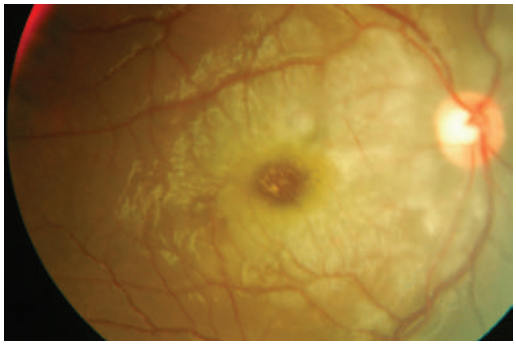


Fig - 3

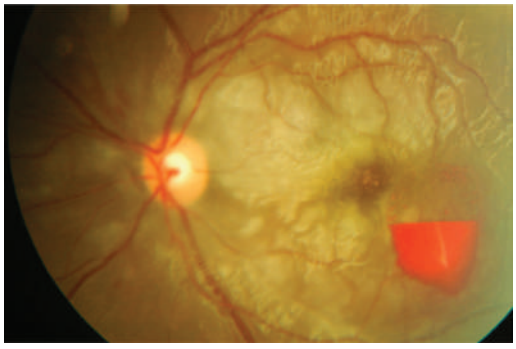


Fig - 4

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- Head trauma. [2]
- Long bone fracture.[4,5]
- Compressive Injuries of trunk & Barotrauma[4]
- Acute pancreatitis[6]
- Child birth.[8]
- Renal Failure.[9]
- Steroid injections in and around the eye & nasal passages. [10]
- Retrobulbar anesthesia .[11]
- Connective tissue and vasculitic diseases.[12]
- SLE,TTP
- HELLP syndrome
- Amniotic fluid embolism.
- Purtschers retinopathy is usually bilateral, but can also be unilateral.Decreased vision occurs in the affected eyes, generally in the range of 20/200 to counting fingers. Vision may improve gradually depending on the severity of the retinal changes. Purtscher's retinopathy associated with pre ecclampsia has demonstrated a poor visual outcome. [8]

Pathophysiology

The exact pathogenesis of Purtschers retinopathy still remains controversial and various hypotheses have been put forward.

1. Purtscher described the white retinal patches (Purtscher's flecken) as intraretinal changes resulting from extravasation of lymph from the retinal vessels due to sudden increase in intracranial pressure during severe head injury.

2. The most accepted mechanism is the complement activation induced leukoembolization. Activation of complement C5a following trauma, acute pancreatitis and vasculitic diseases, leads to aggregation of granulocytes leading to arterial occlusion and infarction of the micro vascular bed.

3. Fat embolism in cases of long bone fractures and pancreatitis from enzymatic digestion of omental fat, amniotic fluid embolism at the time of child birth or postpartum also leads to infarction of the retina

4. Other mechanism is angiospasm, caused by acute rise in venous pressure from compressive chest injuries and head injuries, resulting in endothelial cell damage due to sudden rise in intraluminal pressure.

Clinical features

The patients present with sudden or gradual, unilateral or bilateral loss of vision. Fundus examination shows cotton-wool spots due to obstruction in the axoplasmic flow. Large areas of retinal whitening, having typical polygonal shape with small strips of clearing adjacent to large retinal blood vessels, termed Purtscher's flecken are characteristic. Intraretinal or pre retinal hemorrhages are also noticed. Rarely optic disc edema can occur. After 4 to 6 weeks the white retinal patches fade away and eventually the fundus may appear normal, though there may be residual pigmentary mottling and optic atrophy

Fluoroscein Angiography is often not indicated. It is reported to show features like capillary non-perfusion, late leakage from injured retinal vessels, retinal or disc edema and perivascular staining.

Treatment

Hyperbaric oxygen , intravenous methyl prednisolne , sub tenon Triamcinolone etc have been tried as treatment options. [13, 14, 15] Investigating for the underlying cause and treatment of the same whenever possible should be done wherever indicated. No treatment has been proven to be superior to observation for Purtscher's retinopathy. Spontaneous visual recovery of at least two Snellen lines has been reported in 50% of the cases. There is some evidence that poor initial and final acuities may be associated with persistent acute changes in the retina.(3)

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Brief Report

Primary Iris Cyst: A Case Report

Girija K MS

Primary iris cysts are relatively uncommon and are usually stationary . They are asymptomatic and do not require treatment except in rare instances. They are usually detected during routine slit lamp examination. Rarely peripheral cysts can cause angle closure glaucoma.

CASE REPORT

A 47 year old male presented with complaints of defective vision of five months duration . There was history of a shadow appearing before the right eye on going out into bright sunlight. The shadow was progressively increasing in size.

There was no history of pain, redness, ocular trauma or any ocular surgeries. There was no history of any systemic illness.

General and systemic examinations were normal. The best corrected visual acuity was 6/6, N6 both eyes. Anterior segment on slit lamp examination in the right eye (RE) showed an irregular anterior chamber which was shallow temporally. A smooth dark brown cystic lesion of around 2.5-3mm extending from 4-10 o'clock position, arising from the undersurface of iris, a part of which was seen in the pupillary area was seen inferotemporally (fig.1). Left eye (LE) showed a much smaller similar lesion in the infero-temporal pupillary area extending from 4-5 o'clock position (fig.2). Pupil was normal in size, shape and reaction. Fundus was normal in both eyes. IOP was 17 mm both eyes.

Anterior segment OCT (AS OCT) of both eyes showed cysts arising from posterior surface of iris extending into the pupillary area in both eyes (fig.3).

A diagnosis of mid-zonal primary pigment epithelial cyst of iris was made.

The patient was having visual complaints only in RE as the cyst was larger and was jutting out of the pupillary area encroaching the visual axis. The cyst in the RE was treated with YAG laser. Settings were same as in iridotomy, ie. 3-5 mJ. With 2-3 shots , the cyst wall ruptured. The cyst completely disappeared with a little pigment dispersion into the anterior chamber. Topical steroids and beta blockers were given for a week. Patient was reviewed after 1 week, 1 month and 3 months. The eyes were quiet on all visits and cyst could not be seen on slit lamp or AS OCT. The visual disturbance was relieved.

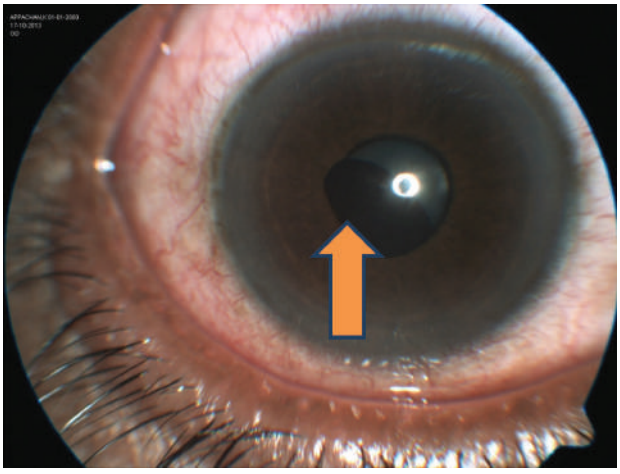


Fig 1 - IRIS CYST RE

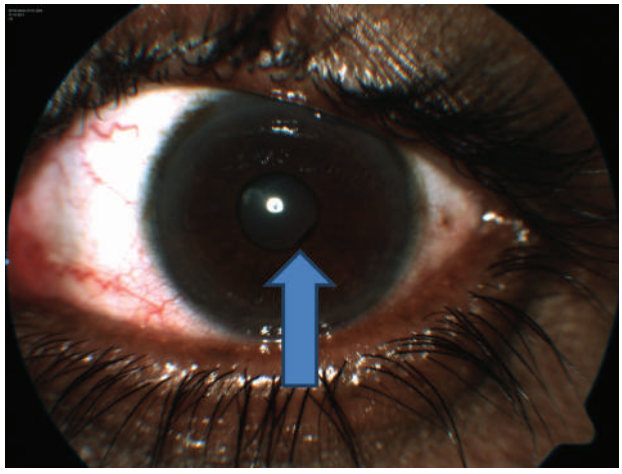


Fig 2 - IRIS CYST LE

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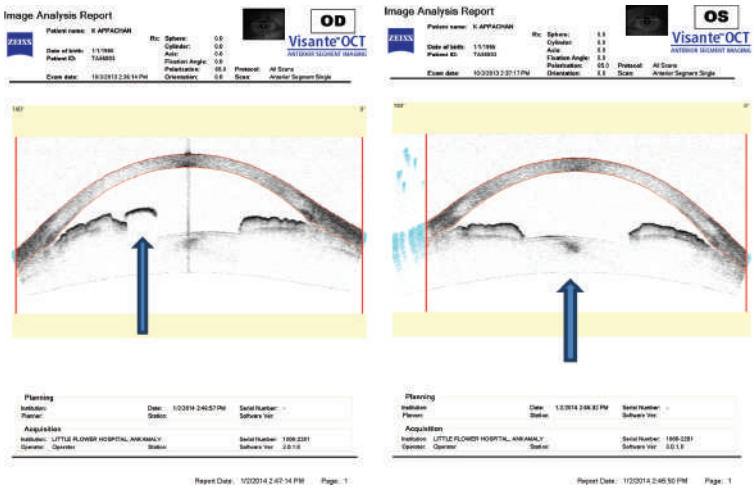


Fig 3 - AS OCT

DISCUSSION

A primary iris cyst is an epithelial-lined space which involves a portion of the iris and which has no recognizable etiology.[2] Secondary iris cysts follow surgical or non-surgical trauma. They frequently enlarge and lead to severe complications such as inflammation and glaucoma.

Primary iris cysts are divided into epithelial and stromal categories[1], each having different clinical characteristics. Epithelial cysts arise between the pigmented epithelial layers of the iris and are classified according to their anatomic location into central cysts (occur at the pupillary margin), midzonal cysts (in the mid-portion of the iris) and peripheral cysts (in the iridociliary sulcus). In some cases, the cysts apparently break free from their epithelial attachment and migrate into the anterior chamber or vitreous chamber (dislodged cysts).

Primary stromal cysts occur within the iris stroma and are not directly continuous with the posterior epithelium. They apparently arise from ectopic surface epithelium which is trapped in the iris during embryologic development.

A great majority of primary iris cysts, particularly those which arise from the iris pigment epithelial layer, are stationary lesions which rarely progress or cause visual complications and hence do not require any treatment.

Peripheral iris cysts sometimes lift the iris forward and cause angle closure glaucoma without pupillary block (pseudoplateau iris). These can be punctured with Argon or Nd:YAG laser[3].

Primary stromal cysts, usually recognized in infancy, are generally progressive, and require treatment by aspiration, cryotherapy or surgical resection.

The differential diagnosis includes iris melanoma, ciliary body melanoma and other rare tumors which arise from the iris stroma like leiomyoma, melanocytoma etc., malignant melanoma and secondary iris cysts.

In case of stromal tumors, slit lamp examination reveals a distinct mass involving the iris stroma that can be directly visualized in the anterior chamber. Some of the ciliary body tumors like medulloepithelioma can present like a peripheral iris cyst, but can be differentiated by UBM.

Iris cyst in the angle differs from a melanoma by its smooth, rounded borders and by the fact that it does not blend into, but rather displaces the iris stroma posteriorly. A nevus or melanoma in the angle is more sessile and is directly continuous with the iris stroma.

Malignant melanomas are solid, rather than cystic on slit lamp examination. Patients with secondary iris cysts usually have a history of surgical or non-surgical ocular trauma and frequently develop glaucoma, corneal edema and other complications.

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Brief Report

Isolated Benign Unilateral Abducent Nerve Palsies in Young Children - A Case Series

Sanitha Sathyan DNB, Meena C.K DNB, Elizabeth Joseph K MS

ABSTRACT

Aim: To report a case series of benign isolated abducent nerve palsies, in 6 children, diagnosed in 2 months at a tertiary care centre from within an area of 30 square km.

Methods: This retrospective case series includes 6 patients < 18 months of age with acute onset abducent nerve palsy, who presented during a period of 2 months. There was no history of prior trauma/ neurological disease. The mean deviation was 40 prism diopters and there was -3 to -4 limitation of abduction in the involved eyes. All underwent MRI brain, which was normal.

Results: All the patients had partial recovery within 2-5 days and total recovery in 10-14 days after treatment with oral steroids.

Conclusion: This case series supports the entity of benign idiopathic sixth nerve palsy and emphasizes on the importance of supportive treatment in otherwise asymptomatic young children. Key words: Abducent palsy, children, isolated

Introduction

Acute onset sixth nerve palsy in a child raises suspicion of serious neurological disease like raised intracranial pressure, pontine glioma and meningitis. However, benign self resolving sixth nerve palsies are also reported. In 1967, Knox, Clark, and Schuster[1] reported a series of 10 children with spontaneous sixth cranial nerve paralysis that occurred about 7 to 21 days after a nonspecific illness. Symonds[2] , Bixenman and Von Noorden et al[3] also have reported isolated self resolving abducent nerve palsies. Acquired sixth nerve palsies following immunisation have also been reported.[4,5] Clustering of the cases of acute abducent nerve palsies have not been reported in literature so far.

Materials and Methods

We report a retrospective case series of 6 patients < 18 months of age, who presented within a period of 2 months, with acute onset of sixth nerve palsy, which resolved with supportive therapy.

All the patients presented to us with acute onset deviation of eyes and associated face turn to the same side, within 2 days of onset of symptoms. Mean age was 13.83 months (10 – 18 months). There was no history of trauma, documented fever, previous ocular deviations or neurological disease.

The mean deviation by the Modified Krimsky test was 40 prism diopters (30-60 prism diopters) and there was -3 to -4 limitation of abduction in the involved eyes. Cycloplegic refraction, anterior segment and fundus examinations were otherwise normal.

All the patients had normal neurological evaluation including MRI brain and were started on oral prednisolone (1 mg/ kg body weight), which was tapered over 4 weeks, with a presumed etiology of transient neuritis of the abducent nerve.

Results

All the patients had partial recovery within 2-5 days and total recovery with a mean of 13.66 days (10-14 days). (ref: Table:1)

Table:1 Clinical profile of patients:

Case	Age (months)	Esotropia (prism diopters)	Partial recovery (days)	Total Recovery (days)
1	10	60	2	10 (recurrence 2 months later)
2	11	40	5	14
3	12	30	3	10
4	18	40	3	14
5	14	40	2	10
6	18	30	3	14

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One child had a second episode of acute onset sixth nerve palsy in the same eye 2 months after the steroids were weaned off. MRI brain was normal in this episode also and the patient was restarted on oral steroids. Partially recovery was seen in 3 days and total recovery in 7 days.

Discussion

Benign self resolving unilateral sixth nerve palsy in young children is a relatively rare diagnosis.

The etiology of benign, self resolving, unilateral sixth nerve palsies remain uncertain and none of the published literature points to a definitive cause. The major predisposing conditions listed in the series by Knox et al[1] included viral infection, otitis media and thrombosis of the inferior petrosal sinus. Symonds et al[2] postulated that since the sixth nerve and the inferior petrosal sinus pass through a tightly fitting dural sheath of Dorello's canal, the compression of the nerve could readily occur if the sinus becomes thrombosed. Functional recovery of the sixth nerve may occur with organization and canalization of the clot .

A case of recurrent sixth nerve palsy in a child of 5 episodes was reported by Bixenman and Von Noorden et al[3], indicating a viral neuritis. They postulated that benign sixth nerve palsy of childhood may have the same immunological basis similar to post-infectious processes like Guillian-Barre syndrome. With recovery from the initial episode, the abducens nerve may have become predisposed to recurrent inflammatory episodes, triggered by febrile illnesses. Acquired sixth nerve palsies after immunisation have also been reported.[4,5]

All these cases reported in our series in children less than 18 months of age were seen in a period of 2 months and 4 of the cases were reported from an area of 30 square kilometres, which points toward a probable infective etiology. Though there was no definite history of viral infection or trauma, the relatively benign course with recovery within 2 weeks suggest a transient neuritis of the sixth nerve, probably triggered by an insignificant viral infection. Also the one recurrent case of sixth nerve palsy suggests a possible immunological basis as proposed by Bixenman and Von Noorden et al.[5]

Though we could not suggest a definitive etiological diagnosis, all the patients in our series were empirically treated with systemic steroids with full recovery within 2 weeks. This report is in favour of the entity called benign idiopathic sixth nerve palsy and emphasizes on the importance of avoiding invasive procedures like lumbar puncture in otherwise asymptomatic infants.

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PG Tear Sheet

Newer Drugs in Glaucoma

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Introduction

The primary goal of glaucoma therapy is to stop the loss of retinal ganglion cells,by rescuing injured cells or regenerating new,functional cells,to replace those that are lost.The classical antiglaucoma drugs are used to reduce intraocular pressure(IOP),arguably the most important risk factor for glaucomatous optic neuropathy.Although reducing IOP is often efficacious,in many cases achieving an appropriate target IOP for an individual patient,may not halt progression.In thelate 1970's "neuroprotection" was introduced as a concept whose principle function is to protect retinal ganglion cells(RGC), utilizingapproaches in addition to modulating IOP.

CLASSIFICATION OF OCULAR HYPOTENSIVE AGENTS

1) Natural products: Cannabinoids
2) Activators of extracellular matrix hydrolysis: Matrix metalloproteinases (MMPs)
3) Cytoskeleton modulator:Ethacrynic acid
4) Protein kinase inhibitors:
5) Compounds that increase cyclic GMP
6) Neuroprotectors

1. CANNABINOIDS:

Mechanism of action:

a) Vasodilation of efferent vessels of anterior uvea.
b) Modification of surface membrane glycoprotein residues in the ciliary epithelium.
c) Increased facility of outflow.

The pharmacology of the cannabinoids[1] includes the cannabinoid(CB) receptors Type 1 and Type 2 or CB1 and CB2,respectively,transporters and enzymes that break down these molecules.The CB1 receptors are present in the ciliary body of humans and rats.

Side effects: Tachycardia, euphoria, hypotension, conjunctival hyperemia ,pulmonary fibrosis and impaired neurological behavior.In particular the most disturbing side effect is hypotension which may be associated with reduced perfusion of the optic nerve head and could be detrimental in protecting against progressive atrophic optic neuropathy. These side effects of cannabinoids seriously limit their use in the treatment of glaucoma.

2) Activators of extracellular matrix hydrolysis group:

Mechanism of action:An excessive accumulation of extracellular matrix material in the trabecular meshwork(TM) of glaucomatous eyes likely contributes to decreased aqueous outflow.Therefore therapeutic manipulations that eliminate the excessive ECM should theoretically improve outflow facility and consequently lower IOP.

Current drug inder study from this group:

a)MMPs:Activation of these enzymes reduces the excessive accumulation of ECM molecules, such as proteoglycans, collagens, fibronectins and laminin in the glaucomatous eye and inturn decreases hydrodynamic resistance of the outflow pathway.

Disadvantages:MMPs being proteins of large molecular mass are not practical as medical treatment>

b)Inducers of MMPs:Tert-butyhydroquinone can upregulate MMP3 expression in the TM cells and increase aqueous outflow facility in glaucoma.

c)Activators of glycosaminoglycan degradation products: Products that catalyse the hydrolysis of GAGs stimulate the degradation of ECM in the TM.GAG degrading enzymes,hyaluronidase and chondroitinase decrease IOP in study models consistently.Similar to MMPs,these enzymes are also not practical for clinical use,as they are larger molecules.

3)Cellular cytoskeleton modulators

Ethacrynic acid is the protype agent in this group.It is a sulfhydryl reactive diuretic that disrupt the cytoskeleton

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(microfilaments, microtubules,intermediate filaments),which is thought to alter TM shape and these changes may be sufficient to alter the local geometry of the outflow pathway,and consequently increase aqueous outflow.

Drugs under study from this group:
a) Ethacrynic acid
b) Latrunculin B
c) Swinholide A

Disadvantages: Poor corneal penetration, corneal toxicity and TM toxicity mainly for ethacrynic acid.Latrunculins does not adversely affect the cornea and hence is now in clinical trials.

4)Protein kinase inhibitors:

Mechanism of action: Exact mechanism is not fully understood. They likely increase the aqueous outflow by affecting cytoskeleton of TM or Schlemm's canal endothelial cells.

Drugs under study
a)Rho kinase Inhibitors
b)Broad spectrum kinase inhibitors H-7
c)Inhibitors of protein kinase c

Rho-kinase inhibitors: There are 2 kinds of Rho kinases[7], ROCK1 and ROCK2, which are serine-threonine kinases that are downstream effectors of Rho GTPase.They regulate smooth muscle contraction in a calcium independent manner.By targeting ROCK activity in the aqueous humour outflow pathway with selective inhibitors,outflow facility through TMis increased leading to decreased IOP.Several ROCK inhibitors(INS117548,DE-104,RK1983)are in clinical trials.

5)Componds that increase cGMP:

Mechanism of action: cGMP affects both aqueous production and outflow. Activation of GMP dependent protein kinases, which by phosphorylation,leads to functional changes of various proteins.eg:an inhibition of Na-K ATPase,leads to decrease in aqueous production.

Drugs under study from this group:
a) Nitric oxide(NO) donors:Nitroglycerine,Isosorbid e dinitrate,sodium nitrite,hydralazine,minoxidil, sodium nitroprusside.
b) Natriuretic peptides:Atrial natriureticpeptide (ANP) ,Brain derived natriuretic peptide(BNP),C-type natriuretic peptide.
c) cGMP analogues:Cell permeable analogues of cGMP.

Intracellular cGMP can also be increased by activation of guanyl cyclases.Nitric oxide(NO) and compounds that release NO(NO donors) are activators of soluble guanyl cyclases. Both NO donors and natriuretic peptides are effective IOP lowering compounds.

6)Neuroprotectors:

Rationale for use of neuroprotectors: It has been hypothesized that intravitreal or intraretinal glutamate levels that are neurotoxic to ganglion cells play a role in glaucoma and hence drugs which work against these agents can help in glaucoma management.They are also supposed to enhance the vascular supply and decrease proapoptotic factors.

Drugs under study from this group:
a)Glutamate receptor antagonist:NMDA receptor antagonist-Memantine.
b)Calcium channel blocker-Nimodipine[2]
c)Alpha agonists-Brimonidine
c)Neurotrophic factors-Neurotrophin 3
d)Apoptotic inhibitors:Cytochrome c release inhibitors,caspase inhibitors
e)NO synthase inhibitors:aminoguanidine

a) Memantine[4]- N Methyl D Aspartate(NMDA) receptor antagonist :
Mechanism of action:The NMDA receptor is an ion channel that is activated by glutamate,allowing extracellular calcium to enter the cell.In normal physiological conditions,the NMDA receptor has an important role in neurophysiological precess such as memory.However excessive activation of the NMDA signaling cascade leads to "excitotoxicity" wherein intracellular calcium overload neurons and causes cell death through apoptosis.Memantine blocks the excessive glutamate stimulation of NMDA receptor of the regional ganglion cells and protects it from calcium mediated apoptosis.

Uses:To treat CNS disorders like Parkinson disease, Alzheimers disease.Currently being studied as a neuroprotective agent in glaucoma.

b)Calcium channel blockers:
NImodipine:produces vasodilation by inhibiting entry of calcium into vascular smooth muscle cells.Hence may protect the optic nerve head by improving vascular perfusion. But the systemic side effects of CCBs does not support the use of this class of drugsfor the routine management of glaucoma.

c)Neurotrophic factors: Neurotrophins[3] are peptides that have an important role in development and maintenance of various neuronal population. Protein derived neurotrophic factor neurotrophin 3 and nerve growth factor have differential effects in the cell survival promotion, differentiation or demise. The role of these biologically active peptides and their receptors in relation to survival and death of ganglion cells is under study.

d)Apoptosis Inhibitors:Caspases are family of proteasesthat executing the dismantling ond demolition of cells undergoing apoptosis.Caspases 8 and 9 have been shown to be activated in experimental glaucoma. Suppression of apoptosis using caspases inhibitors is an approach that has been explored with modest success.

e)Nitric oxide synthase Inhibitors:
Aminoguanidine:NO is a gaseous second messenger molecule.It has both physiological and pathologic fuction in blood flow,immune response and neuronal communication. The expression of NO is regulated by 3 different forms of NO synthase(NOS)-Endothelial NOS(eNOS),Neuronal NOS(nNOS),inducible NOS(iNOS).

Role of NO in eye:Excessive NO generated by iNOS in optic nerve astrocytes and microglia are associated with optic nerve damage. Aminoguanidine, by inhibiting iNOS was shown to prevent retinal ganglion cell loss.

IMMUNOMODULATION

It has been proposed that immune system plays a key role in the ability of optic nerve and retina to withstand glaucoma. The mechanism involves recruitment of both innate and adaptive immune cells that together create aprotective nishe to halt progression of glaucoma.eg:therapeutic vaccination with glatiramer acetate(cop1).

Other newer agents:

1)Tetrahydro cortisol: A metabolite of cortisol shown to lower the dexamethasone induced ocular hypertension.

2)MIfepristone: Aspecific glucocortocoid receptor antagonist lowers IOP.

3)Spiranolactone:A synthetic steroidal aldosterone antagonist with potassium sparing diuretic action,produces significant lowering of IOP in glaucoma patients.

4)Antazoline:An antihistamine,shown to lower the IOP following topical administration apparently by decreasing aqueous production.

5)Melatonin:A pineal hormone that reduces IOP.
Demeclocycline,a tetracycline derivative also lowers IOP by reducing aqueous production.

6)Ginkgobiloba extract: Leaf extracts of the ginkgo tree have many neuroprotective properties applicable to the treatment of non IOP dependent risk factors for glaucomatous damage. IT exerts significant protective effects against free radical damage and lipid peroxidation.It can scavenge NO and also reduce glutamate induced elevation of calcium concentration and inhibits apoptosis.It also preserves mitochondrial metabolism.

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Fathima Benazir DO, DNB

Role of Corneal Collagen Cross-Linking in Pseudophakic Bullous Keratopathy A Clinicopathological Study

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Ophthalmology. 2013: 120 (12); 2413-18

The aim of this study was to evaluate the clinical and histopathologic changes induced by collagen cross-linking (CXL) in pseudophakic bullous keratopathy (PBK)

This was a randomized, prospective, interventional study. Twenty-four patients with corneal edema resulting from PBK of more than 4 months' duration and awaiting keratoplasty were enrolled to undergo CXL followed by penetrating keratoplasty. They were allocated randomly into 2 groups of 12 patients each. 12 patients underwent penetrating keratoplasty 1 month after CXL (group A), whereas the remaining 12 patients underwent penetrating keratoplasty 3 months after CXL (group B). The primary outcome of the study was the effect on visual acuity, ocular discomfort (tearing, redness, and pain), corneal haze, central corneal thickness, (CCT), ocular discomfort, and histopathologic modifications of corneal stroma at 1 or 3 months after CXL. The corneal buttons underwent histopathologic and Immunofluorescence evaluation.

Mean visual acuity showed a significant improvement after CXL, from 1.925$\pm$0.173 before surgery to 1.75$\pm$0.296 at 1 month after surgery (P = 0.010), but deteriorated to 1.81$\pm$0.23 at 3 months. The mean VAS scores of patients in both groups showed a statistically significant decrease at 1 week &1 month though it showed a worsening trend at 3 months it was still significantly lower than the preoperative value. A trend of reduction in corneal haze was noted in group A and group B after CXL The effect was maintained in 9 patients in group B at 3 months. The mean central corneal thickness decreased significantly from 846.46$\pm$88.741 to 781.0$\pm$98.788 mm at 1 month (P$<$0.01) after CXL, but increased to 805.08$\pm$136.06 mm at 3 months. Immunofluorescence microscopy revealed anterior stromal compaction in 7 of 12 patients (58.3%) in group A and in 5 of 12 patients (41.6%) in group B. Staining of keratocyte revealed a relative uniform distribution throughout the stroma an intact epithelium in all samples, suggesting that the epithelium had regrown in all cases after CXL

In this study it was found that visual analog scales depicting ocular discomfort improved in both groups maximum being at 1 month. Visual analog scale scores at 3months, although greater than those at 1 month, were still lower than the preoperative values. This symptomatic relief probably resulted from CXL-induced stromal compaction and reduced bullae formation. The decrease in CCT could be attributed to the cross linking effect causing compaction in the early period, but the effect was not long lasting, probably because of decreased riboflavin diffusion across the highly edematous corneas.

CXL-induced stromal compaction is more evident in moderate compared with advanced stages of the disease and this probably was the result of reduced riboflavin diffusion into the thicker stroma. A limitation of the study is that patients with early manifestation of PBK were not included. So corneal CXL can be considered as a new tool in the armamentarium for the temporary reduction in corneal edema in patients with bullous keratopathy awaiting keratoplasty.

The Effect of Phacoemulsification on Intraocular Pressure in Medically Controlled Open-Angle Glaucoma Patients

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Am J Ophthalmol 2014;157:26–31

This study was aimed to evaluate intraocular pressure (IOP) after phacoemulsification in patients with medically controlled open-angle glaucoma (OAG), and examine the association of biometric variables to IOP changes.

It was a retrospective case series. Medically well controlled open-angle glaucoma patients without prior incisional glaucoma surgery undergoing phacoemulsification by a single surgeon between January 1997 and October

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2011 were evaluated. Patient charts were reviewed to obtain demographic information, preoperative glaucoma medications, severity and treatment measures, and preoperative and postoperative IOP. Patients were identified who showed lowered or stable IOP at 1 year without any increase in medications or additional laser trabeculoplasty vs those who required additional medications or laser for IOP control, or whose IOP was higher after surgery with the same medication regimen. Additional analysis of patients who had no change in their medication regimen during the year following surgery regardless of their IOP response to phacoemulsification (n = 102) was also assessed.

A total of 157 eyes (157 patients) were included in the study. The average preoperative IOP of 16.3 ± 3.6 mm Hg decreased to 14.5 ± 3.4 mm Hg at 1 year (P < .001). Sixty eyes (38%) required additional medications or laser for IOP control within the first year postoperatively, or had a higher IOP at postoperative year 1 without medication change. Among eyes without postoperative medication changes (n = 102), higher preoperative IOP (P <0 .001), older age (P = 0.006), and deeper anterior chamber depth (P=0.015) were associated with lower postoperative IOP.

In this study they found out the single greatest predictor of IOP change was the level of preoperative IOP, also a deeper anterior chamber preoperatively was associated with a greater IOP lowering effect after surgery when controlling for age and preoperative IOP. Though phacoemulsification resulted in a small average decrease in IOP in patients with POAG, a sizeable proportion of medically controlled glaucoma patients with open angles undergoing phacoemulsification experienced an increase in IOP or required more aggressive treatment to control IOP postoperatively. They were unable to detect any additional patient characteristics that might help predict which eyes will or will not obtain an IOP reduction from cataract surgery.

Strategy for the Management of Uncomplicated Retinal Detachments.

The European Vitreo-Retinal Society RetinalDetachmentStudyReport1

Ron A. Adelman, Aaron J. Parnes, Didier Ducournau

Ophthalmology. 2013: 120 (9); 1804-08

Objective of this study was to analyze the surgical strategy in RRD repair and success and failure in the treatment of uncomplicated rhegmatogenous retinal detachments (RRDs). The optimal treatment of rhegmatogenous retinal detachment (RRD) has been debated for decades. Retrospective and prospective studies in the literature, while demonstrating the overall high anatomic success rate of all methods, do not provide a consensus regarding the best procedure in terms of outcome. This study has the largest report of the treatment of retinal detachment in the literature.

It was a nonrandomized, multicenter retrospective study. One hundred seventy-six surgeons from 48 countries spanning 5 continents provided information on the primary procedures for 7678 cases of RRDs including 4179 patients with uncomplicated RRDs. Reported data included specific clinical findings, the method of repair, and the peri and postoperative complications. Main Outcome Measures were final failure of retinal detachment repair that is detached retina judged to be inoperable (level 1 failure rate), remaining silicone oil at the study's conclusion (level 2 failure rate), and recurrence of the detachment and need for additional procedures to repair the detachment (level 3 failure rate)

4179 uncomplicated cases of RRD were included. Combining phakic, pseudophakic, and aphakic groups, those treated with scleral buckle alone (n = 1341) had a significantly lower final failure rate than those treated with vitrectomy, with or without a supplemental buckle (n = 2723; P = 0.04). When comparing those who underwent vitrectomy alone (without buckle) with those who underwent a scleral buckle procedure alone, the level 1 failure rate was not statistically significantly different(P=0.134). In phakic patients, final failure rate was lower in the scleral buckle group compared with those who had vitrectomy, with or without a supplemental buckle (P = 0.028). In pseudophakic patients, the failure rate of the initial procedure was lower in the vitrectomy group compared with the scleral buckle group (P = 3x10-8). There was no statistically significant difference in failure rate between segmental (n = 721) and encircling (n = 351) buckles (P =0.5). Those who underwent vitrectomy with a supplemental scleral buckle (n = 488) had an increased failure rate compared with those who underwent vitrectomy alone (n = 2235; P = 0.048). Pneumatic retinopexy was found to be comparable with scleral buckle when a retinal hole was present (P = 0.65), but not in cases with a flap tear (P = 0.034).

So to conclude from this study, in uncomplicated phakic eyes, scleral buckle alone can be considered as a good option. However, in pseudophakic eyes, there is no clear winner and the surgeon should consider higher risk of level 3 failure with scleral buckle versus higher risk of level 2 failure with vitrectomy. However, if a vitrectomy is to be

performed, these data suggest that a supplemental buckle is not helpful. There was no significant difference between segmental versus 360-degree buckle. Pneumatic retinopexy may be considered in cases of retinal detachment with grade 0 or grade A PVR and atrophic holes.

Limitation of this study has been that it had failure as a primary outcome measure instead of final visual acuity which would have been more enlightening. Another limitation is the short follow-up period. It is likely that level 2 failure rates would fall if the patients were followed up for longer periods. However it is a large scale study with participation of large number of surgeons from 48 countries with wide variety of techniques so that results are applicable to retinal surgeons worldwide.

Strategy for the Management of Complex Retinal Detachments

The European Vitreo-Retinal Society Retinal Detachment Study Report 2

Ron A. Adelman, Aaron J. Parnes, Jack O. Sipperley, Didier Ducournau

Ophthalmology. 2013: 120 (9); 1809-13

Objective of this study was to analyze the outcome of the treatment of complex rhegmatogenous retinal detachments (RRDs).Even though several retrospective and prospective studies have been done in the past no consensus has been reached regarding the optimal treatment of complex retinal detachment in each clinical situation. This is the largest study of its kind in the literature. Here they discuss the results of the treatment of RRDs in those eyes with PVR (grade B or grade C-1), choroidal detachment, significant hypotony, large or giant retinal tears, and macular holes.

Nonrandomized, multicenter, retrospective study. One hundred seventy-six surgeons from 48 countries spanning 5 continents reported primary procedures for 7678 RRDs. Reported data included clinical manifestations, the method of repair, and the outcome. Main Outcome Measures were failure of retinal detachment repair detached retina judged to be inoperable (level 1 failure rate), remaining silicone oil at the study's conclusion (level 2 failure rate), and recurrence of the detachment or need for additional procedures to repair the detachments (level 3 failure rate).

The main categories of complex retinal detachments evaluated in this investigation were: (1) grade B proliferative vitreoretinopathy (PVR; n=917), (2) grade C-1 PVR (n=637), (3) choroidal detachment or significant hypotony (n=578), (4) large or giant retinal tears (n=1167), and (5) macular holes (n=153). In grade B PVR, the level 1 failure rate was higher when treated with a scleral buckle alone versus vitrectomy (P=0.0017). In grade C-1 PVR, there was no statistically significant difference in the level 1 failure rate between those treated with vitrectomy, with or without scleral buckle, and those treated with scleral buckle alone (P=0.7). The level 2 failure rate was substantially higher in the group who received a vitrectomy and had a high rate of remaining silicone oil (P=0.0015). Vitrectomy with a supplemental buckle had an increased failure rate compared with those who did not receive a buckle (P=0.007).Cases with choroidal detachment or hypotony treated with vitrectomy had a significantly lower failure rate versus treatment with scleral buckle alone (P=0.0015). Large or giant retinal tears treated with vitrectomy also had a significantly lower failure rate versus treatment with scleral buckle (P=7x10-8). There was no statistically significant difference in level 1 failure rate between tamponade with gas versus silicone oil in all the groups. In the macular hole group vitrectomy alone was used and here too no statistically significant difference in level 1 failure rate between tamponade with gas versus silicone oil was found.

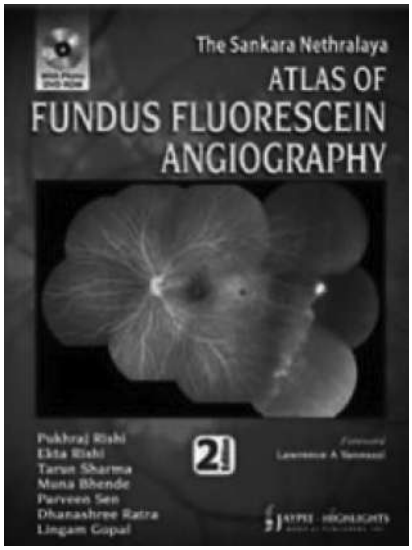
The study results show that in grade B PVR, choroidal detachment, significant hypotony, a large tear, or a giant tear, vitrectomy is the procedure of choice. When grade C-1 PVR is present, no significant difference in the level 1 failure rate is seen when comparing vitrectomy with scleral buckle. Tamponade with either gas or silicone oil was comparable, although level 2 failure was high with silicone oil. In those detachments with grade C-1 PVR or large or giant retinal tears treated with vitrectomy, it seems that a supplemental scleral buckle may not be advantageous and actually may be associated with a higher level 1 failure rate than if vitrectomy alone is performed.

Limitations of this study was the usage of attachment of retina rather than final visual acuity as the primary outcome measure and short follow up time that tend to push up the numbers of level 2 failure. Additional prospective, randomized studies are needed to determine optimal treatment for these types of retinal detachments and to confirm these results.

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THE SANKARA NETHRALAYA ATLAS OF FUNDUS FLUORESCEIN ANGIOGRAPHY

Authors: Pukhraj Rishi, Ekta Rishi, Tarun Sharma, Muna Bhende, Parveen Sen, Dhanashree Ratra, Lingam Gopal
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Publisher: Jaypee-Highlights Medical Publishers, Inc.
Number of Pages: 624



Sankara Nethralaya, Chennai, is one of the leading ophthalmic institutions of Asia. This book, comprising original data from this institute is a comprehensive reference guide to the fluorescein angiographic findings of different disorders.

The book is divided into seven sections, and subdivided into relevant chapters. The first section is an introduction to fluorescein angiography, while the remaining six sections are based on different clinical groupings.

The chapters are very well laid out in an easy to read format. The illustrations are of a uniformly high standard and presented as interesting case studies with colour fundus photographs in addition to the fluorescein angiography pictures. Though the text is kept to a minimum, there is adequate description of the clinical and angiographic features of the cases presented. Of note are the comments and clinical nuggets at the end of each chapter which provide interesting take home messages. At the end of the clinical sections is a glossary of useful fluorescein angiography terms. The addition of the index which was absent in the previous edition has made this book more useful allowing easy reference to specific conditions without leafing through each section.

This book is not intended to be a retinal textbook but is an atlas of retinal disorders illustrated with great clinical photographs. Very useful for postgraduates and fellows is the 'Self-Test' chapter at the end of the book, which provides a quick revision of the topics covered. Overall, this book is a very well illustrated atlas of fundus fluorescein angiography covering a wide range of fundus disorders and would be a valuable addition to every ophthalmic library.

NEW TRENDS IN OPHTHALMOLOGY – MEDICAL AND SURGICAL MANAGEMENT

Author: Samuel Boyd, Benjamin F. Boyd
Publishing Year: 2013
Publisher: Jaypee – Highlights Medical Publishers, Inc.
Pages: 335



New Trends in Ophthalmology comprehensively covers the most recent technological developments in the rapidly advancing field of ophthalmology. There are 26 chapters, each with excellent illustrations, especially of the surgical techniques. International contributors cover the latest diagnostic and therapeutic approaches in the field.

Following a chapter on ocular anatomy and the evaluation

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and treatment of surface diseases and damage, chapters discuss in detail approaches and technologies employed in treating specific congenital and acquired conditions from blepharitis to uveitis. Surgical advances including that for pterygium to vitreoretinal surgery have been covered extensively with excellent illustrations. The book also includes results of imaging studies, clinical trials and treatment guidelines.

Presented in an easy to follow format, this comprehensive manual is enhanced by nearly 400 clinical photographs, diagrams and tables. For practicing ophthalmologists and ophthalmic residents alike, this book is an invaluable text for updating themselves in our ever advancing field of ophthalmology.

EYE DOCTOR OUT OF THE BOX



Author: Dr. Itteyerah Tholath
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ISBN - 9781301878284

A book with a difference, by one of our very own stalwarts in ophthalmology, Dr. T. P. Itteyerah.

Old age and death are unsolved problems of humanity. This book is an outcome of the thought process of Dr. Itteyerah on these unsolved problems.

The book is spread out in 5 chapters and explores the existing imaginations and knowledge in eliminating old age and death. There is a proposal for a scientific method to convert the dream to a reality. It tries to analyze the different types of obstacles in achieving an old age free world.

This unique book is a cocktail of facts and fiction to intoxicate the reader with the ideas of eternal youth and escape from death. It contains a brilliant but apparently impossible idea to bypass old age and death, thereby changing the whole life cycle of humans on the globe.

This book is a description of a genuinely big dream of a doctor published in an environment friendly digital form. The book is easily accessible through any common search engine (Google, Yahoo or Microsoft Bing). It can be viewed in HTML and could be downloaded in Kindle, Epub, PDF, RTF, LRF, PDB or in plain text format.

Dear editor,

I am indeed happy to see the editorship of Journal of K.S.O.S.(Kerala Journal of ophthalmology) coming back to Little Flower Hospital, which had several past editors right from the day K.S.O.S. was formed. In fact the journal started as a bulletin with a single issue in an year. Later it has grown and transformed to the present status due to the efforts of several past editors of this journal. However there is scope for lot of further improvements. I am sure you shall utilize all the modern techniques in bringing out the journal good in appearance as well as in content.

Generally when a journal becomes popular it will get good original articles .Even reprinting good articles from other important journal with their permission should be considered in the initial period if there is shortage of good articles. In a professional journal nothing can substitute original good quality articles.

Today the technology to document cases is easily available. Accessibility to publications on any subject is at your finger tip. What is lacking is the will to write articles. I feel it is the duty of the editor to stimulate and encourage the members to write good articles. You should make them realize that in modern days 'if you do not publish you shall perish'.

As you know change is the only thing that is not changing. Change and transformation is essential for progress. We follow classifications, concepts about disease process, and protocols of treatment as per internationally accepted norms. But the journal as an instrument for change should encourage to question these standards with rational thinking. We should transform the learned members of the society from the status of strong followers of change to initiators of change. This is the only way our members shall be noticed internationally. Please look at what has happened in the management of peptic ulcers of stomach. Anybody with rational thinking can think that an ulcer could be caused by bacteria. But we had to wait more than a century for an Australian pathologist to announce to the world that he has found the bacteria responsible for gastric ulcers. We never questioned the traditional concept that gastric and duodenal ulcers are caused by hydrochloric acid. If we had questioned the concept with common sense we could have looked for the bacteria or any other organism in the ulcer. We can invent things accidentally if you have good observational qualities. But this happens only once in a blue moon as it happened in the discovery of penicillin. If you have something in your mind and look for it you may find many more things needed to be changed and ripe for a change. The journal should make people to look for areas of change and should share their dreams about the anticipated change. Once you have a dream you have something to work on. Remember when you dream never be stingy or miserly about it. Always think big and have a big dream.

Review articles, case reports, P.G. section, photo essay, Quiz, book review etc also are very important part of the journal. You may encourage members to give feed backs as letters to the editor so that you know how you are being assessed by the readers. This feedback is very important for further improvement and of the journal.

Wishing you a very fruitful period of editorship of KJO.

Dr. Ittyerah.T.P.
Former editor, Journal of K.S.O.S. & Indian Journal of Ophthalmology.